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=> fil cancer drugu drugb pascal jic biotechno esbio caba biotechds lifesci biosis
toxcenter wpids uspatf scisearch; d que l98; fil embase; d que l25; d que l34; fil medl;
d que l3
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L84      126175 SEA (NERVE OR NEURON?)(2A) (GROWTH FACTOR#) OR NEUROTROPHIC
                FACTOR# OR NEUROTROPIN# OR NEUREGULIN# OR GLIAL MATURATION
                FACTOR#
L85       34503 SEA SUBLINGUAL?
L88          44 SEA L84(S) L85
L93        3830 SEA L85(3A) GLAND#
L94       11318 SEA L85(5A) ADMIN?
L95        2917 SEA L85(5A) DOS####
L96          17 SEA L88 NOT L93
L97           8 SEA L88 AND (L94 OR L95)
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nerve growth factor
+
sublingual admin

L98 17 SEA (L96 OR L97)

FILE 'EMBASE' ENTERED AT 13:03:33 ON 20 AUG 2004

FILE COVERS 1974 TO 19 Aug 2004 (20040819/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L24 18154 SEA FILE=EMBASE ABB=ON NEUROTROPHIC FACTOR+NT/CT
L25 0 SEA FILE=EMBASE ABB=ON L24(L)LI/CT
LI = sublingual administration

L24 18154 SEA FILE=EMBASE ABB=ON NEUROTROPHIC FACTOR+NT/CT
L32 3610 SEA FILE=EMBASE ABB=ON SUBLINGUAL DRUG ADMINISTRATION/CT NOT LI/CT
L33 6964 SEA FILE=EMBASE ABB=ON L24(L)EC/CT - EC = endogenous compound
L34 2 SEA FILE=EMBASE ABB=ON L24 AND L32 NOT L33

FILE 'MEDLINE' ENTERED AT 13:03:35 ON 20 AUG 2004

FILE LAST UPDATED: 19 AUG 2004 (20040819/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L1 17224 SEA FILE=MEDLINE ABB=ON NERVE GROWTH FACTORS+NT/CT
L2 978 SEA FILE=MEDLINE ABB=ON ADMINISTRATION, SUBLINGUAL/CT
L3 0 SEA FILE=MEDLINE ABB=ON L1 AND L2

=> dup rem l98,l34
FILE 'DRUGU' ENTERED AT 13:03:44 ON 20 AUG 2004

FILE 'BIOTECHNO' ENTERED AT 13:03:44 ON 20 AUG 2004

FILE 'CABA' ENTERED AT 13:03:44 ON 20 AUG 2004

FILE 'BIOTECHDS' ENTERED AT 13:03:44 ON 20 AUG 2004

FILE 'LIFESCI' ENTERED AT 13:03:44 ON 20 AUG 2004

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FILE 'USPATFULL' ENTERED AT 13:03:44 ON 20 AUG 2004

FILE 'EMBASE' ENTERED AT 13:03:44 ON 20 AUG 2004

PROCESSING COMPLETED FOR L98
PROCESSING COMPLETED FOR L34
L99 16 DUP REM L98 L34 (3 DUPLICATES REMOVED)
ANSWER '1' FROM FILE DRUGU
ANSWER '2' FROM FILE BIOTECHNO
ANSWERS '3-8' FROM FILE BIOTECHDS
ANSWERS '9-11' FROM FILE WPIDS
ANSWERS '12-14' FROM FILE USPATFULL
ANSWERS '15-16' FROM FILE EMBASE

=> d ibib ed ab 1-16

L99 ANSWER 1 OF 16 DRUGU
ACCESSION NUMBER: 2002-24562 DRUGU T
TITLE: Emerging therapies in the pharmacological treatment of Parkinson's disease.
AUTHOR: Korczyn A D; Nussbaum M
CORPORATE SOURCE: Univ.Tel-Aviv
LOCATION: Ramat Aviv, Isr.
SOURCE: Drugs (62, No. 5, 775-86, 2002) 1 Tab. 115 Ref.
CODEN: DRUGAY ISSN: 0012-6667
AVAIL. OF DOC.: Department of Neurology, Sackler School of Medicine, Tel-Aviv University Medical School, Ramat-Aviv 69978, Israel. (e-mail: neuro13@post.tau.ac.il).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The emerging therapies in the pharmacological treatment of Parkinson's disease are reviewed. Increasing dopaminergic stimulation with dopamine agonists, catechol O-methyltransferase inhibitors and dopamine reuptake inhibitors is discussed. The modulation of non-dopaminergic systems is considered. The neuroprotection provided by antioxidants, MAO-B inhibitors, and N-methyl-D-aspartate antagonists is addressed. The potential therapies for rescue of dopaminergic cells using antiinflammatory agents, neurotrophic growth factors, and protein antiaggregants are described. The role of genetic factors and gene therapy is illustrated. In spite of all these new and exciting developments, almost half of patients with Parkinson's disease use some form of alternative medical therapy. Thus, there is still a long way ahead to control, and hopefully to prevent, this chronic debilitating disease.

L99 ANSWER 2 OF 16 BIOTECHNO
DUPLICATE
ACCESSION NUMBER: 1985:15226863 BIOTECHNO
TITLE: Nerve growth factor in mouse milk during early lactation: Lack of dependency on submandibular salivar glands
AUTHOR: Grueters A.; Lakshmanan J.; Tarris R.; et al.

CORPORATE SOURCE: Department of Pediatrics, Harbor-UCLA Medical Center, Torrance, CA 90509, United States.
SOURCE: Pediatric Research, (1985), 19/9 (934-937)
CODEN: PEREBL
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
ED 20000202
AB Using a specific and sensitive **nerve growth factor** radioimmunoassay we show measurable quantities of .beta. **nerve growth factor** in mouse milk during the period of early lactation. Partial purification by cationic exchange resin yielded a preparation which exhibited biological activity in a PC-12 cell bioassay system. Submandibular-**sublingual** sialoadenectomy had no influence on the breast milk NGF concentrations. These results support the presence of bioactive NGF in mouse milk during early lactation, but do not clarify the source.

L99 ANSWER 3 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-04223 BIOTECHDS
TITLE: New composition comprising neuregulin (NRG), nucleic acid encoding NRG or an agent that enhances the production and/or function of NRG, and a therapeutic agent, useful for treating or preventing heart diseases, e.g. viral myocarditis; involving vector-mediated gene transfer and expression in host cell for use in therapy
AUTHOR: ZHOU M
PATENT ASSIGNEE: ZENSUN SHANGHAI SCI TECH LTD
PATENT INFO: WO 2003099300 4 Dec 2003
APPLICATION INFO: WO 2003-CN355 15 May 2003
PRIORITY INFO: WO 2002-349 24 May 2002; WO 2002-349 24 May 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-042705 [04]
AB DERWENT ABSTRACT:
NOVELTY - A combination comprising: (a) a **neuregulin** (NRG) protein, a nucleic acid encoding NRG protein, their functional fragment, or an agent that enhances production and/or function of NRG; and (b) a prophylactic or therapeutic agent for viral myocarditis, dilated (congestive) cardiomyopathy (DCM), or myocardial infarction.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a method for preventing, treating or delaying viral myocarditis, DCM, cardiac toxicity or myocardial infarction in a mammal by administering a NRG protein, a nucleic acid encoding the protein, their functional fragment, or an agent that enhances production and/or function of NRG; (2) a pharmaceutical composition for preventing, treating or delaying viral myocarditis or DCM in a mammal comprising a NRG protein, a nucleic acid encoding a NRG protein, their functional fragment, or an agent that enhances production and/or function of NRG; (3) a kit comprising the combination above or the composition in a container, and an instruction for using the combination in preventing, treating or delaying viral myocarditis, DCM or myocardial infarction; and (4) a pharmaceutical composition for preventing, treating or delaying a disease in a mammal comprises a safety dosage equal to or less than about 170 U/kg, or in a total regimen equal to or less than about 3600 U/kg.

ACTIVITY - Cardiant. Descending limb of coronary was ligated with non-invasive sutures at the site between left auricle and pulmonary cone. After about 6 days, when ejection fraction of the left ventricle decreased by about 50%, animals were divided in 3 (10-13 animals/group). Animals were injected with recombinant human NRG1beta into the tail vein with either 5, 10 or 20 mug/kg of NRG 1 for 10 consecutive days. Heart function determination was performed 6 days before and after drug

administration. After consecutive 5-day of drug administration in 3 dosage levels groups of NRG1beta, ejection fraction and shortening fraction of the animals were increased respectively. changes of ejection fraction in 20 mug/kg group maintained for about 35 days after drug administration. There was also significant reduction in ischemic area of the myocardium, increase capillary number of the fibrotic lesion, reduced peripheral angiotensin I, angiotensin II and aldosteron levels.

MECHANISM OF ACTION - ErbB2-ErbB4 receptor agonist.

USE - The combination is useful for preventing, treating or delaying viral myocarditis, DCM, cardiac toxicity or myocardial infarction. NRG can be used to repair damaged myocardial cell structure, strengthen connection between these cells, improve myocardial function and strengthen myocardial biological effect.

ADMINISTRATION - Dosage is about 25-25000 microg of the NRG protein, nucleic acid encoding the NRG protein, or their functional fragment (claimed). Administration can be oral, rectal, topical, inhalational, buccal, **sublingual**, or parenteral (e.g. subcutaneous, intramuscular, intradermal or intravenous).

EXAMPLE - Total RNA and mRNA were extracted from brain tissue of a 5-month human fetus and reversibly transcribed to cDNA. RT-PCR was performed with the transcribed cDNA as template and a pair of primers to amplify target gene. PCR product was examined in electrophoresis on 1.5% agarose. Specific 183 bp DNA fragment was found and the length of which was the same as anticipated. (146 pages)

L99 ANSWER 4 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-02988 BIOTECHDS
TITLE: Promoting neural growth in the central nervous system of a mammal comprising administering a combination of neurotrophins capable of enhancing neurite outgrowth in an amount to promote neural growth;
neural growth promotion and vector expression in host cell for use in gene therapy
AUTHOR: LOGAN A; BERRY M
PATENT ASSIGNEE: LOGAN A; BERRY M
PATENT INFO: US 2003121064 26 Jun 2003
APPLICATION INFO: US 2002-293573 13 Nov 2002
PRIORITY INFO: US 2002-293573 13 Nov 2002; US 1997-49286 11 Jun 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-863455 [80]
AB DERWENT ABSTRACT:

NOVELTY - Promoting neural growth in vivo in the central nervous system of a mammal comprises administering to the mammal a combination of at least 2 neurotrophins capable of enhancing neurite outgrowth, or its active fragments, cognates, congeners, mimics, analogues, secreting cells and soluble molecules, in an amount to promote the neural growth, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a recombinant DNA molecule for use in the above method, comprising 2 or more of the above neurotrophins, or its active fragments, cognates, congeners, mimics or analogues, associated with an expression control sequence; (2) a vector comprising the recombinant DNA molecule; (3) a transformed host containing the vector; (4) a pharmaceutical composition for modulating neural growth in the CNS of a mammal, comprising an amount of the above combination and a pharmaceutical carrier; (5) a transgenic mammal comprising secreting cells which express 2 or more neurotrophins; (6) a cell culture comprising the fibroblast cells of the transgenic mammal; (7) a cell culture system comprising tissue from the CNS of the mammal; and (8) a method for enhancing neural outgrowth of CNS neurons, comprising culturing the neurons on the cell culture system.

BIOTECHNOLOGY - Preferred Method: In promoting neural growth in vivo in the central nervous system of a mammal, the neurotrophins are

nerve growth factor, acidic or basic fibroblast growth factor, neurotrophin-3 or brain-derived **neurotrophic factor**. The neurotrophins are delivered to the CNS via secreting cells that express the factors. The secreting cells are transfected fibroblasts expressing the factors. The method further comprises administering a **nerve growth factor**

.

ACTIVITY - Neuroprotective; Nootropic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful in promoting neural growth in vivo in mammalian CNS to enable the damaged or diseased nerve to again function.

ADMINISTRATION - The neurotrophins are administered via perineural route (claimed). Other means of **administration** include **sublingual**, rectal, nasal, intraventricular, intracerebral, oral or parenteral delivery. No dosage given.

EXAMPLE - No relevant example given.(17 pages)

L99 ANSWER 5 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-09738 BIOTECHDS
TITLE: New composition for modulating immune responses, comprises a vascular endothelial growth factor (VEGF), an immunomodulating protein, and/or a nucleic acid encoding VEGF or the protein that is operably linked to regulatory elements

;

vector-mediated gene transfer and expression in host cell for vaccine, immunotherapy and gene therapy

AUTHOR: WEINER D B; SIN J
PATENT ASSIGNEE: UNIV PENNSYLVANIA; WEINER D B; SIN J
PATENT INFO: WO 2002100345 19 Dec 2002
APPLICATION INFO: WO 2002-US18541 11 Jun 2002
PRIORITY INFO: US 2001-297336 11 Jun 2001; US 2001-297336 11 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-156910 [15]

AB DERWENT ABSTRACT:

NOVELTY - A composition for modulating immune responses comprises: (a) vascular endothelial growth factor (VEGF) and/or at least one nucleic acid molecule that encodes VEGF operably linked to regulatory elements; and (b) at least one immunomodulating protein and/or at least one nucleic acid molecule that encodes at least one immunomodulating protein operably linked to regulatory elements.

DETAILED DESCRIPTION - The immunomodulating protein is selected from granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-12, IL-15, IL-2, B7.1, B7.2, MCP-1, MIP-1alpha, MIP-1beta, IL-8, RANTES, L-selectin, P-selectin, E-selectin, CD34, GlyCAM-1, MadCAM-1, LFA-1, VLA-1, Mac-1, p150.95, PECAM, ICAM-1, ICAM-2, ICAM-3, CD2, LFA-3, M-CSF, G-CSF, IL-4, mutant forms of IL-18, CD40, CD40L, vascular **growth factor**, IL-7, **nerve growth factor**, Fas, TNF receptor, Flt, Apo-1, p55, WSL-1, DR3, TRAMP, Apo-3, AIR, LARD, NGRF, DR4, DR5, KILLER, TRAIL-R2, TRICK2, DR6 and Caspase ICE. INDEPENDENT CLAIMS are included for: (1) a cell comprising the above nucleic acid molecule; (2) a pharmaceutical composition comprising the above composition; (3) methods for enhancing or suppressing immune response in an individual, comprising administering to the individual the above composition; (4) a method for inducing an immune response in an individual against an immunogen, comprising administering to the individual the composition cited above; (5) a recombinant vaccine comprising the above composition; (6) a method for inducing apoptosis in a target cell population in an individual, comprising administering to the individual the above composition, where the cell-specific ligand is specific for the target cell population; and (7) a vector for gene

therapy, comprising the above nucleic acid molecule in a vector suitable for the transformation of mammalian cells.

ACTIVITY - Immunosuppressive; Immunostimulant; Cytostatic; Antiinflammatory; Antirheumatic; Antiarthritic; Dermatological; Antipsoriatic; Neuroprotective; Antithyroid. No biological data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The composition is useful for immunotherapy, as well as, for enhancing, suppressing, or otherwise modulating immune responses in conjunction with vaccine delivery. The methods are used for preventing and/or treating individuals with cancer and autoimmune diseases, such as rheumatoid arthritis, multiple sclerosis, autoimmune thyroiditis, scleroderma, psoriasis, and Crohn's disease.

ADMINISTRATION - Administration is by intramuscular, intranasal, intraperitoneal, intradermal, subcutaneous, intravenous, intraarterial, intraocular, oral, topical, transdermal, inhalational or suppository or to mucosal tissue such as by lavage to vaginal, rectal, urethral, buccal and **sublingual** tissue. No **dosage** given.

EXAMPLE - No relevant examples given. (24 pages)

L99 ANSWER 6 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-14748 BIOTECHDS
TITLE: Screening granulocyte colony stimulating factor (G-CSF) analogs useful in treating e.g. neutropenia, comprises determining the ability of a G-CSF analog to stimulate proliferation of target cells at an initial ligand concentration;
involving vector-mediated gene transfer and expression in host cell for use in drug screening and hematopoietic disorder, neurological disorder, reproductive disease, immune disease, infectious disease, bone disease, anemia and AIDS therapy and gene therapy
AUTHOR: SARKAR C A; LAUFFENBURGER D A
PATENT ASSIGNEE: AMGEN INC
PATENT INFO: WO 2002020767 14 Mar 2002
APPLICATION INFO: WO 2000-US28828 8 Sep 2000
PRIORITY INFO: US 2000-231464 8 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-415730 [44]
AB DERWENT ABSTRACT:

NOVELTY - Screening analogs (M1) of granulocyte colony stimulating factor (G-CSF) for use as G-CSF replacements or antagonists, comprises determining the capacity of the G-CSF analog to stimulate cellular proliferation of target cells at a given initial ligand concentration, is new.

DETAILED DESCRIPTION - Screening analogs (M1) of granulocyte colony stimulating factor (G-CSF) for use as G-CSF replacements or antagonists, comprises determining the capacity of the G-CSF analog to stimulate cellular proliferation of target cells at a given initial ligand concentration. The methods comprising: (1) screening analogs of Granulocyte Colony Stimulating Factor (G-CSF) for use as G-CSF replacements, comprising: (a) determining the capacity of the G-CSF analog for binding to target cells and determining an equilibrium dissociation constant (Kd) for the analog; (b) determining the capacity of the G-CSF analog for stimulating cellular proliferation (N) of target cells at a given initial ligand concentration (L); (c) normalizing the N value obtained for the G-CSF analog with the corresponding N value for wild-type G-CSF at a given value of L to obtain Y-axis values; (d) calculating the L/Kd values for the G-CSF analog and wild type G-CSF to obtain X-axis values; (e) plotting the normalized N value with the L/Kd values for the G-CSF analog and wild-type G-CSF; and (f) selecting as a G-CSF replacement, an analog displaying increased proliferation and

either increased or decreased binding relative to wild-type G-CSF; (2) screening analogs of G-CSF for use as G-CSF antagonists, comprising: (1) determining the capacity of the G-CSF analog for binding to target cells and determining an equilibrium dissociation constant (Kd) for the analog; (2) determining the capacity of the G-CSF analog for stimulating cellular proliferation (N) of target cells at a given initial ligand concentration (L); (3) normalizing the N value obtained for the G-CSF analog with the corresponding N value for wild-type G-CSF at a given value of L to obtain Y-axis values; (4) calculating the L/Kd values for the G-CSF analog and wild type G-CSF to obtain X-axis values; (e) plotting the normalized N value with the L/Kd values for the G-CSF analog and wild-type G-CSF; and (5) selecting as a G-CSF antagonist an analog displaying decreased proliferation and either equal or increased binding relative to wild-type G-CSF. INDEPENDENT CLAIMS are also included for the following: (1) treating (M2) hematopoietic, neurological or reproduction conditions, or sensitizing cells to chemotherapy and radiotherapy by administering a G-CSF replacement; (2) treating neutrophilia by administering a G-CSF antagonist; (3) culturing (M3) hematopoietic cells in vitro; (4) a kit (I) containing components for culturing hematopoietic cells comprising: (a) a polypeptide analog produced by (M1'); (b) components for preparing medium for culturing hematopoietic cells; and (c) optionally, at least one additional factor selected from erythropoietin (EPO), G-CSF, stem cell factor (SCF), megakaryocyte growth and differentiation factor (M-GDF), granulocyte-macrophage colony-stimulating factor (GM-CSF), macrophage-coolony stimulating factor (M-CSF), CSF-1, interleukins (IL) IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-I1, IL-12, insulin like growth factor (IGF-1), leukemia inhibitory factor (LIF), interferons, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor.

BIOTECHNOLOGY - Preferred Method: The condition consists of reduced hematopoietic function, reduced immune function, reduced neutrophil count, reduced neutrophil mobilization, mobilization of peripheral blood progenitor cells, sepsis, severe chronic neutropenia, bone marrow transplants, infectious diseases, leucopenia, thrombocytopenia, anemia, enhancing engraftment of bone marrow during transplantation, enhancing bone marrow recovery in treatment of radiation, chemical or chemotherapeutic induced bone marrow aplasia or myelosuppression, and acquired immune deficiency syndrome. The target cell is a bone marrow stem cell, a neutrophil precursor cell, an immortalized stem cell, or an acute myeloid leukemia cell. Cellular proliferation is assessed by determining cell number, measuring 3H-thymidine incorporation, or using an 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. The equilibrium dissociation constant (Kd) is assessed by BIAcore analysis or enzyme-linked immunoabsorbent assay (ELISA). Culturing hematopoietic cells in vitro comprises placing the cells in culture medium containing a G-CSF replacement selected from: (Glu50)G-CSF, (Glu54)G-CSF, (Ala33)G-CSF, (Glu26)G-CSF, (Asp30)G-CSF, (Leu26)G-CSF, (Ala38)G-CSF, (Ala26)G-CSF, and the Met-1 species, and providing suitable conditions for the growth of the hematopoietic cells. Sensitizing or culturing cells in vitro includes using at least one additional factor selected from EPO, G-CSF, SCF, M-GDF, GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-I1, IL-12, Interleukins, IGF-1, LIF, interferon, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor. Preferred Replacements: The G-CSF replacements may be selected from (Glu50)G-CSF, (Glu54)G-CSF, (Ala33)G-CSF, (Glu26)G-CSF, (Asp30)G-CSF, (Leu26)G-CSF, (Ala38)G-CSF, (Ala26)G-CSF, and the Met-1 species.

ACTIVITY - Immunostimulant; hemostatic; antianemic; antibacterial; immunosuppressive; anti-HIV; osteopathic. No suitable data given.

MECHANISM OF ACTION - G-CSF agonist.

USE - The method is useful for screening G-CSF analogs which can be used to treat hematopoietic neurological, or reproduction related

conditions, including reduced hematopoietic function, immune function, neutrophil count or neutrophil mobilization, mobilization of peripheral blood progenitor cells, sepsis, severe chronic neutropenia, bone marrow transplants, infectious diseases, leucopenia, thrombocytopenia, anemia, enhanced engraftment of bone marrow during transplantation, enhanced bone marrow recovery in treatment of radiation, chemical or chemotherapeutic induced bone marrow aplasia or myelosuppression, and acquired immune deficiency syndrome. G-CSF analogs may be also used in replacement therapy protocols for the treatment of neutropenia, and in gene therapy.

ADMINISTRATION - The G-CSF analogs may be administered through oral, nasal, pulmonary, topical, intravenous, intradermal, intramuscular, intramammary, intraperitoneal, intrathecal, retrobular, intrapulmonary, **sublingual**, anal, vaginal or transdermal routes. **Dosage** is 0.001-1000 mug/kg body weight per day.

ADVANTAGE - The G-CSF analog polypeptides demonstrate advantages in stability, which are not seen in other G-CSF species, and provide enhanced cellular response (superagonist or G-CSF agonist type activity) compared to G-CSF or metG-CSF.

EXAMPLE - Granulocyte colony stimulating factor (G-CSF) analogs were prepared by either insertional or site-directed mutagenesis of DNA encoding r-met-HuG-CSF using the polymerase chain reaction (PCR) overlap extension method. After confirming mutations by sequence analysis, each of the mutants was expressed in E. coli K12, refolded, and purified. The DNA encoding recombinant human G-CSF had an initial methionine codon followed by codons for the 174-amino acid species of human G-CSF. The purified r-met-HuG-CSF analogs retain the initiating Met (position Met-1). Confirmation of the identity of the G-CSF analogs was accomplished by N-terminal amino acid sequencing of intact proteins. Sequences of the purified G-CSF analogs matched the sequences predicted from the respective DNA sequences. (66 pages)

L99 ANSWER 7 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-14747 BIOTECHDS
TITLE: New human granulocyte colony stimulating factor analogs comprising a substitution of aspartic acid with histidine at amino acid residues 109, 112 or 119, useful for in replacement therapy protocols for treating e.g. neutropenia; virus vector or plasmid-mediated gene transfer and expression in Escherichia coli, mammal, cancer, yeast or insect cell or hematopoietic stem cell for use in therapy and gene therapy
AUTHOR: SARKAR C A; LAUFFENBURGER D A; TIDOR B
PATENT ASSIGNEE: AMGEN INC
PATENT INFO: WO 2002020766 14 Mar 2002
APPLICATION INFO: WO 2000-US28602 8 Sep 2000
PRIORITY INFO: US 2000-231464 8 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-415729 [44]
AB DERWENT ABSTRACT:

NOVELTY - A human granulocyte colony stimulating factor (G-CSF) analog polypeptide (I) comprising an amino acid substitution, is new.

DETAILED DESCRIPTION - A human granulocyte colony stimulating factor (G-CSF) analog polypeptide (I) comprises an amino acid substitution in the fully defined 174 amino acid sequence given in the specification, selected from a substitution of aspartic acid with histidine at position 109, (His 109)G-CSF; at position 112, (His112)G-CSF; at position 119 (His119)G-CSF; or any of their subparts optionally including an N-terminal methionyl residue. INDEPENDENT CLAIMS are also included for the following: (1) a G-CSF analog polypeptide of claim I derivatized with one or more water-soluble polymers; (2) a polynucleotide encoding (I); (3) an expression construct containing a polynucleotide of (2); (4) a

host cell containing a polynucleotide of (2); (5) a process for producing G-CSF analog polypeptides (His109)G-CSF, (His112)G-CSF, (His119)G-CSF, or the Met-1 species, from a host cell containing nucleic acid encoding such analogs, by culturing the host cell containing (I) to facilitate the expression of the polypeptide, and obtaining the G-CSF analog polypeptide; (6) a method (M1) of treating a hematopoietic, neurological or reproduction related condition by administering a composition comprising (I) to the patient; (7) a method (M2) of sensitizing cells to chemotherapy and radiotherapy by administering a composition comprising (I) to a patient; (8) a method (M3) for culturing hematopoietic cells in vitro by placing the cells in a culture medium containing a G-CSF analog polypeptide, and growing hematopoietic cells; and (9) a kit containing components for culturing hematopoietic cells comprising: (a) an analog polypeptide (I); (b) components for preparing medium for culturing hematopoietic cells; and (c) optionally, at least one additional factor selected from erythropoietin (EPO), G-CSF, stem cell factor (SCF), megakaryocyte-growth and differentiation factor (M-GDF), GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, 11,-9, IL-10, IL-11, IL-12, Interleukins, IGF-1, leukemia inhibitory factor (LIF), interferon, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor.

BIOTECHNOLOGY - Preparation: G-CSF analogs were prepared by either insertional or site-directed mutagenesis of DNA encoding r-met-HuG-CSF using the polymerase chain reaction overlap extension method. Preferred Analog Polypeptide: The G-CSF analog polypeptide is derivatized with one or more water-soluble polymers. Preferred Polynucleotide: The polynucleotide molecule is selected from a DNA comprising: (a) a sequence selected from three fully defined 565 nucleotide sequences given in the specification, or their complements; and (b) any of the DNA sequences of subpart (a) additionally encoding an N- terminal methionyl residue. Preferred Host Cell: The host cell is a bacterium, mammalian, cancer, yeast, or insect cell. Preferred Method: In M1 and M2, treatment, and sensitizing or culturing of cells further includes the use of at least one additional factor selected from EPO, G-CSF, SCF, M-GDF, GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, Interleukins, IGF-1, LIF, interferon, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor.

ACTIVITY - Immunostimulant; hemostatic; antianemic; antibacterial; immunosuppressive; anti-HIV; osteopathic.

MECHANISM OF ACTION - G-CSF agonist.

USE - The G-CSF analogs are useful for treating hematopoietic, neurological or reproduction related conditions, including reduced hematopoietic function, immune function, neutrophil count or neutrophil mobilization, mobilization of peripheral blood progenitor cells, sepsis, severe chronic neutropenia, bone marrow transplants, infectious diseases, leucopenia, thrombocytopenia, anemia, enhanced engraftment of bone marrow during transplantation, enhanced bone marrow recovery in treatment of radiation, chemical or chemotherapeutic induced bone marrow aplasia or myelosuppression, and acquired immune deficiency syndrome. G-CSF analogs may be also used in replacement therapy protocols for the treatment of neutropenia, and in gene therapy setting. DNA sequences are useful in generating new and useful viral and plasmid DNA vectors and host cells.

ADMINISTRATION - Administration is by intravenous, intradermal, intramuscular, intramammary, intraperitoneal, intrathecal, retrobulbar, intrapulmonary, oral, **sublingual**, nasal, anal, vaginal or transdermal delivery, or by surgical implantation at a particular site. Dosage is 0.001-1000 microg/kg body weight per day.

ADVANTAGE - The G-CSF analog polypeptides demonstrate advantages in stability, which are not seen in other G-CSF species, and provide enhanced cellular response (superagonist or G-CSF agonist type activity) as compared to wild type G-CSF.

EXAMPLE - Granulocyte colony stimulating factor (G-CSF) analogs were prepared by either insertional or site-directed mutagenesis of DNA encoding r-met-HuG-CSF using the polymerase chain reaction overlap extension method. After confirming mutations by sequence analysis, each of the mutants was expressed in Escherichia coli K12, refolded, and purified. The DNA encoding recombinant human G-CSF had an initial methionine codon followed by codons for the 174-amino acid species of human G-CSF. The purified r-met-HuG-CSF analogs retain the initiating Met (position Met-1). Each of the G-CSF analogs with a substitution of aspartic acid with histidine at position 109, (His 109)G-CSF, at position 112, (His112)G-CSF, and at position 119 (His119)G-CSF, comprises a fully defined sequence of 565 nucleotides encoding a protein having a sequence of 174 amino acids given in the specification. Confirmation of the identity of the G-CSF analogs was accomplished by N-terminal amino acid sequencing of intact proteins. Sequences of the purified G-CSF analogs matched the sequences predicted from the respective DNA sequences. (69 pages)

L99 ANSWER 8 OF 16 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-09639 BIOTECHDS
TITLE: Screening Granulocyte Colony Stimulating Factor (G-CSF) analogs for treating e.g. sepsis or anemia, comprises determining the capacity of a G-CSF analog to stimulate proliferation of target cells at a given ligand concentration ; cell culture for disease therapy
AUTHOR: SARKAR C A; LAUFFENBURGER D A
PATENT ASSIGNEE: SARKAR C A; LAUFFENBURGER D A
PATENT INFO: US 2002151488 17 Oct 2002
APPLICATION INFO: US 2001-950473 10 Sep 2001
PRIORITY INFO: US 2001-950473 10 Sep 2001; US 2000-231464 8 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-198331 [19]
AB DERWENT ABSTRACT:
NOVELTY - Screening analogs of Granulocyte Colony Stimulating Factor (G-CSF) for use as G-CSF replacements or G-CSF antagonists comprising determining the capacity of the G-CSF analog for stimulating cellular proliferation of target cells at a given initial ligand concentration, is new.

DETAILED DESCRIPTION - Screening analogs of G-CSF for use as G-CSF replacements or G-CSF antagonists comprises: (a) determining the capacity of the G-CSF analog for binding to target cells and determining an equilibrium dissociation constant (Kd) for the analog; (b) determining the capacity of the G-CSF analog for stimulating cellular proliferation (N) of target cells at a given initial ligand concentration (L); (c) normalizing the N value obtained for the G-CSF analog with the corresponding N value for wild-type G-CSF at a given value of L to obtain Y-axis values; (d) calculating the L/Kd values for the G-CSF analog and wild-type G-CSF to obtain X-axis values; (e) plotting the normalized N value with the L/Kd values for the G-CSF analog and wild-type G-CSF; and (f) selecting as a G-CSF replacement, an analog displaying increased proliferation and either increased or decreased binding relative to wild-type G-CSF. INDEPENDENT CLAIMS are also included for the following: (1) treating a hematopoeitic, neurological or reproduction related conditions by administering a G-CSF replacement selected from the novel method; (2) treating neutrophilia by administering a G-CSF antagonist selected from the novel method; (3) sensitizing cells to chemotherapy and radiotherapy by administering a G-CSF replacement selected from the novel method; (4) culturing hematopoietic cells in vitro; (5) a kit containing components for culturing hematopoietic cells comprising: (a) any of the polypeptide analogs selected by the novel method; (b) components for

preparing medium for culturing hematopoietic cells; and (c) optionally, at least one additional factor selected from erythropoeitin (EPO), G-CSF, stem cell factor (SCF), monocyte (M)-CSF, granulocyte monocyte (GM)-CSF, colony stumulating factor (CSF)-1, interleukin (IL)-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, insulin-like growth factor (IGF)-1, leukocyte inhibitory factor (LIF), interferon, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor.

BIOTECHNOLOGY - Preferred Method: In screening analogs for G-CSF, the target cell is a bone marrow stem cell, a neutrophil precursor cell, an immortalized stem cell, or an acute myeloid leukemia cell. Cellular proliferation is assessed by determining the cell number, measuring 3H-thymidine incorporation, or using an MTT assay. The equilibrium dissociation constant (Kd) is assessed by BIAcore analysis or enzyme linked immunosorbent assay (ELISA). Culturing hematopoietic cells in vitro comprises placing the cells in a culture medium containing a G-CSF replacement selected above, and providing suitable conditions for the growth of the hematopoietic cells. The methods of (1), (2) and (3) includes the use of at least one additional factor selected from EPO, G-CSF, SCF, M-GDF, GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, interleukins, IGF-1, LIF, interferon, a **neurotrophic factor**, flt-3/flk-2 ligand, and a fibroblast growth factor. The G-CSF replacement is selected from (Glu50)G-CSF, (Glu54)G-CSF, (Ala33)G-CSF, (Glu26)G-CSF, (Asp30)G-CSF, (Leu26)G-CSF, (Ala38)G-CSF, (Ala26)G-CSF, and the Met-1 species. Treatment of neutrophilia comprises administering (Ala26)G-CSF, and its Met-1 species.

ACTIVITY - Hemostatic; Antianemic; Anti-HIV; Antibacterial; Immunosuppressive; Immunostimulant. No biological data is given.

MECHANISM OF ACTION - None given.

USE - The G-CSF replacements are useful for treating hematopoietic function, reduced immune function, reduced neutrophil count, reduced neutrophil mobilization, mobilization of peripheral blood progenitor cells, sepsis, severe chronic neutropenia, bone marrow transplants, infectious diseases, leucopenia, thrombocytopenia, anemia, enhancing engraftment of bone marrow during transplantation, enhancing bone marrow recovery in treatment of radiation, chemical or chemotherapeutic induced bone marrow aplasia or myelosuppression, and acquired immune deficiency syndrome (claimed).

ADMINISTRATION - Dosage is 1 micro-g/kg-100 mg/kg, preferably 0.1-50 mg/kg. Administration can be intravenous, intradermal, intramuscular, intramammary, intraperitoneal, intrathecal, retrobulbar, intrapulmonary, oral, **sublingual**, nasal, anal, vaginal, or transdermal delivery, or by surgical implantation at a particular site.

EXAMPLE - Granulocyte colony stimulating factor (G-CSF) dependent cells were factor-starved for 24 hours and then incubated with G-CSF or G-CSF analogs (at an initial ligand concentration of 1000, 500, 250 or 125 pM) at an initial density of 1x10 to the power 5 cells/ml. After 7 days, cell number was measured by Coulter counter. Ligand binding affinity of G-CSF analog to G-CSF receptor was measured using a BIAcore (RTM) 2000. Histidine-tagged wild type G-CSF was immobilized on the chip surface, and free receptor was passed over the chip to generate a standard equilibrium curve and to calculate wild-type binding affinity using a 1:1 model. Mutant ligand binding affinity was determined by mixing 2 nM free receptor with a known concentration of mutant ligand and passed over the chip. Mutant equilibrium binding affinities were determined using a 1:1 model with competition. Results show that (Ala33)G-CSF, (Glu26)G-CSF, (Asp30)G-CSF, (Leu26)G-CSF, (Ala38)G-CSF, and (Ala26)G-CSF exhibited enhanced trafficking properties. These G-CSF analogs showed roughly the same binding activity as wild-type and elicited roughly the same cellular proliferation at high ligand concentrations. (25 pages)

L99 ANSWER 9 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER: 2003-576472 [54] WPIDS
CROSS REFERENCE: 2000-431196 [37]
DOC. NO. CPI: C2003-155647
TITLE: Method for diagnosing, preventing or treating central nervous system disorder, involves administering composition comprising agent to tissue innervated by trigeminal nerve and outside nasal cavity.
DERWENT CLASS: A96 B04 B07
INVENTOR(S): FREY, W H; THORNE, R G
PATENT ASSIGNEE(S): (CHIR) CHIRON CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003072793	A1	20030417	(200354)*		21

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2003072793	A1	CIP of	US 1998-208539	19981209
		Cont of	US 1999-458562	19991209
			US 2002-301185	20021121

PRIORITY APPLN. INFO: US 1999-458562 19991209; US 1998-208539 19981209; US 2002-301185 20021121
ED 20030821
AB US2003072793 A UPAB: 20030821
NOVELTY - A method of therapy for a mammal in need of diagnosis, prevention or treatment of a central nervous system disorder, involves administering a composition comprising an agent to a tissue innervated by the trigeminal nerve and outside the nasal cavity of the mammal. The agent is absorbed through the tissue and transported to the central nervous system of the mammal.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for method of transporting an agent to the central nervous system of a mammal, which involves administering a composition comprising the agent directly to a tissue such as skin tissue, mucosa of upper or lower eyelid, oral tissue such as gingival tissue, anterior two-thirds of tongue, mucosa of cheek and mucosa of upper or lower lip.

ACTIVITY - Antidepressant; Antimanic; Antiparkinsonian; Nootropic; Neuroprotective; Cerebroprotective; Tranquilizer; Neuroleptic; Cytostatic; Antibacterial; Antiinflammatory; Anti-HIV.

No test details are given for the above mentioned activity.

MECHANISM OF ACTION - None given.

USE - For treating or preventing neurological condition, psychiatric disorder, infection of central nervous system, disease/damage/inhibiting degeneration of nerve cells in the central nervous system, neurodegenerative disorder, affective disorder, nerve damage due to cerebrovascular disorder, depression, mania, Parkinson's disease, Alzheimer's disease, Lewy body dementia, multiple sclerosis, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, anxiety disorders, schizophrenia, stroke in brain and spinal cord, brain-, spinal cord-tumor, prion disease, anosmia, brain injury, spinal cord injury, meningitis and HIV infection and also provides protective effect on brain cells against stroke (claimed).

ADVANTAGE - Use of neural pathway to transport an agent to the brain,

spinal cord or other components of the central nervous system obviates the obstacle presented by the blood-brain barrier, so that medications like nerve growth factor and protein that cannot normally cross the barrier, can be delivered directly to the brain, cerebellum, brain stem or spinal cord. The delivery of therapeutic agent to the central nervous system by the neural pathway reduces systemic delivery and unwanted systemic side effects.
Dwg.0/0

L99 ANSWER 10 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-398645 [34] WPIDS
DOC. NO. CPI: C1998-120656
TITLE: New 4-substituted gem-di phenyl alkyl-1,2,3,6-tetra hydro-pyridine derivatives - having neurotrophic and neuroprotective activity are useful in treatment of Alzheimer's disease.
DERWENT CLASS: B03
INVENTOR(S): BARONI, M; CARDAMONE, R; FOURNIER, J; GUZZI, U
PATENT ASSIGNEE(S): (SNFI) SANOFI SA; (SNFI) SANOFI-SYNTHELABO
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9825904	A1	19980618	(199834)*	FR	26
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
FR 2757161	A1	19980619	(199834)		
AU 9854895	A	19980703	(199847)		
NO 9902870	A	19990811	(199943)		
CZ 9902110	A3	19990915	(199945)		
EP 950049	A1	19991020	(199948)	FR	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
SK 9900787	A3	19991210	(200008)		
CN 1240428	A	20000105	(200021)		
BR 9713926	A	20000321	(200028)		
US 6124318	A	20000926	(200051)		
HU 2000001437	A2	20000928	(200062)		
NZ 336032	A	20001222	(200104)		
AU 730142	B	20010301	(200117)		
MX 9905468	A1	20000301	(200123)		
KR 2000069421	A	20001125	(200130)		
JP 2001505903	W	20010508	(200131)		28
EP 950049	B1	20011017	(200169)	FR	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
DE 69707504	E	20011122	(200201)		
ES 2167805	T3	20020516	(200239)		
CZ 290242	B6	20020612	(200251)		
NO 313282	B1	20020909	(200266)		
RU 2198874	C2	20030220	(200324)		
SK 283332	B6	20030603	(200345)		
MX 206490	B	20020207	(200362)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9825904	A1	WO 1997-FR2289	19971212

FR 2757161	A1	FR 1996-15336	19961213
AU 9854895	A	AU 1998-54895	19971212
NO 9902870	A	WO 1997-FR2289	19971212
		NO 1999-2870	19990611
CZ 9902110	A3	WO 1997-FR2289	19971212
		CZ 1999-2110	19971212
EP 950049	A1	EP 1997-951326	19971212
		WO 1997-FR2289	19971212
SK 9900787	A3	WO 1997-FR2289	19971212
		SK 1999-787	19971212
CN 1240428	A	CN 1997-180583	19971212
BR 9713926	A	BR 1997-13926	19971212
		WO 1997-FR2289	19971212
US 6124318	A	WO 1997-FR2289	19971211
		US 1999-331005	19990727
HU 2000001437	A2	WO 1997-FR2289	19971212
		HU 2000-1437	19971212
NZ 336032	A	NZ 1997-336032	19971212
		WO 1997-FR2289	19971212
AU 730142	B	AU 1998-54895	19971212
MX 9905468	A1	MX 1999-5468	19990611
KR 2000069421	A	WO 1997-FR2289	19971212
		KR 1999-705202	19990610
JP 2001505903	W	WO 1997-FR2289	19971212
		JP 1998-526323	19971212
EP 950049	B1	EP 1997-951326	19971212
		WO 1997-FR2289	19971212
DE 69707504	E	DE 1997-607504	19971212
		EP 1997-951326	19971212
		WO 1997-FR2289	19971212
ES 2167805	T3	EP 1997-951326	19971212
CZ 290242	B6	WO 1997-FR2289	19971212
		CZ 1999-2110	19971212
NO 313282	B1	WO 1997-FR2289	19971212
		NO 1999-2870	19990611
RU 2198874	C2	WO 1997-FR2289	19971212
		RU 1999-115082	19971212
SK 283332	B6	WO 1997-FR2289	19971212
		SK 1999-787	19971212
MX 206490	B	WO 1997-FR2289	19971212
		MX 1999-5468	19990611

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9854895	A	Based on	WO 9825904
CZ 9902110	A3	Based on	WO 9825904
EP 950049	A1	Based on	WO 9825904
BR 9713926	A	Based on	WO 9825904
US 6124318	A	Based on	WO 9825904
HU 2000001437	A2	Based on	WO 9825904
NZ 336032	A	Based on	WO 9825904
AU 730142	B	Previous Publ.	AU 9854895
		Based on	WO 9825904
KR 2000069421	A	Based on	WO 9825904
JP 2001505903	W	Based on	WO 9825904
EP 950049	B1	Based on	WO 9825904
DE 69707504	E	Based on	EP 950049
		Based on	WO 9825904
ES 2167805	T3	Based on	EP 950049
CZ 290242	B6	Previous Publ.	CZ 9902110

		Based on	WO 9825904
NO 313282	B1	Previous Publ.	NO 9902870
RU 2198874	C2	Based on	WO 9825904
SK 283332	B6	Previous Publ.	SK 9900787
		Based on	WO 9825904

PRIORITY APPLN. INFO: FR 1996-15336 19961213
ED 19980826
AB WO 9825904 A UPAB: 19980826
4-Substituted gem-diphenyl alkyl-1,2,3,6-tetrahydropyridine derivatives of formula (I), their salts, solvates and quaternary ammonium salts are new. Y = CH or N; R1 = halo, CF3, 1-4C alkyl or 1-4C alkoxy; R2, R3 = H or 1-3C alkyl; n = 0 or 1; Ph1, Ph2 = phenyl (optionally mono- or poly-substituted). Also claimed are compositions containing (I) and a compound which is used in the symptomatic treatment of Alzheimer's-type senile dementia.

USE - (I) have neuroprotective and a similar neurotrophic activity to that of **Nerve Growth Factor**. They can re-establish the functioning of damaged cells and those with anomalies in their physiological functioning. They may be used in the event of memory disorders, vascular dementia, post-encephalitic and post-apopleptic disorders, post-traumatic syndromes due to cranial trauma, disorders due to cerebral anoxia, Alzheimer's disease, senile dementia, subcortical disease such as Huntington's chorea and Parkinson's disease, dementia due to AIDS, neuropathies due to sympathic or sensorial nerve damage, cerebral oedema, spinocerebellar or motor neurone degeneration such as lateral amyotrophic sclerosis. **Administration** is oral, parenteral, **sublingual** or transdermal and in a daily dose of 0.25-700 (preferably 1-150) mg.

ADVANTAGE - (I) possess high activity and low toxicity.
Dwg.0/0

L99 ANSWER 11 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1995-005164 [01] WPIDS
DOC. NO. CPI: C1995-001735
TITLE: New quisqualic acid analog - is useful in treatment of e.g. epilepsy, Alzheimer's disease or memory/learning disorders.
DERWENT CLASS: B03
INVENTOR(S): JOHNSON, R L; KOERNER, J F; SUBASINGHE, N L
PATENT ASSIGNEE(S): (MINU) UNIV MINNESOTA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5359087	A	19941025	(199501)*		10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5359087	A	US 1993-72033	19930603

PRIORITY APPLN. INFO: US 1993-72033 19930603
ED 19950110
AB US 5359087 A UPAB: 19950110
Quisqualic acid analog of formula (I) and its salts, are new. In (I), the dotted line represents an opt. second bond; R = H, A, Cy, CyA, allyl, Ar or YO2CA; Y = H, A or Cy; each X = H, A, Ar, CyA' or Cy; A is 1-4C alkyl; Cy = 3-6C cycloalkyl; and Ar = 6-10C aryl.

More specifically, R is H or A esp. H, CH3 or CH2CO2H; Y is H; and X is H.

USE - (I) is useful in treatment of neuronal disorders such as epilepsy, Huntington's chorea, Alzheimer's disease, memory/learning disorders or small/taste disorders. (I) may also be used to enhance the sensitivity of neurons to other bioactive cpds. Such as huperzine A, **neuronal growth factor** or acetyl choline.

Admin. is, e.g., nasal, **sublingual**, buccal, transdermal, vaginal or intravenous. No general dosage details are given.

Dwg.0/2

L99 ANSWER 12 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2004:165919 USPATFULL

TITLE: Method of treatment of psychological conditions by administration of nerve growth factor

INVENTOR(S): McMichael, John, Delanson, NY, UNITED STATES
Unice, Kenneth A., Meadville, PA, UNITED STATES

PATENT ASSIGNEE(S): MILKHAUS LABORATORY, INC., Providence, RI (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004127409	A1	20040701	
APPLICATION INFO.:	US 2003-624328	A1	20030722	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-424443P	20021107 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE, CHICAGO, IL, 60606

NUMBER OF CLAIMS: 28

EXEMPLARY CLAIM: 1

LINE COUNT: 838

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method for administering nerve growth factor to treat various psychological conditions such as of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, and attention deficit syndrome, and alleviate symptoms associated with premenstrual syndrome (PMS), premenstrual dysphoric disorder (PMDD), sleep disorders, tension headaches, and constipation that arise as complications from a psychological condition.

L99 ANSWER 13 OF 16 USPATFULL on STN

ACCESSION NUMBER: 96:116355 USPATFULL

TITLE: Use of excitatory opioid receptor antagonists to prevent growth factor-induced hyperalgesia

INVENTOR(S): Crain, Stanley M., Leonia, NJ, United States
Shen, Ke-fei, Flushing, NY, United States
Kessler, John A., New Canaan, CT, United States
Apfel, Stuart C., West Hempstead, NY, United States

PATENT ASSIGNEE(S): Albert Einstein College of Medicine of Yeshiva University, a Division of Yeshiva University, Bronx, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5585348		19961217	
APPLICATION INFO.:	US 1993-106401		19930813	(8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-17349, filed on 10 Feb 1993, now abandoned And a			

continuation-in-part of Ser. No. US 1993-97460, filed on 27 Jul 1993, now patented, Pat. No. US 5472943
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
ASSISTANT EXAMINER: Touzeau, P. Lynn
LEGAL REPRESENTATIVE: Amster, Rothstein & Ebenstein
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 646
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to a method of preventing hyperalgesia and other undesirable side-effects associated with the administration of growth factor, including nerve growth factor, utilizing an antagonist capable of inactivating excitatory opioid receptor-mediated functions on neurons in the nociceptive pathway. In addition, this invention relates to a composition comprising a growth factor and an antagonist capable of inactivating excitatory opioid receptor-mediated functions on neurons in the nociceptive pathway.

L99 ANSWER 14 OF 16 USPATFULL on STN
ACCESSION NUMBER: 93:62942 USPATFULL
TITLE: Method of ameliorating herpes simplex virus infections using purified nerve growth factor
INVENTOR(S): Wilcox, Christine L., Denver, CO, United States
Johnson, Jr., Eugene M., St. Louis, MO, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5232695		19930803
APPLICATION INFO.:	US 1990-624488		19901206 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1987-137274, filed on 23 Dec 1987, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Moezie, F. T.
LEGAL REPRESENTATIVE: Hastreiter, Roberta L., Matukaitis, Paul D.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treatment are described for use of purified nerve growth factor to ameliorate viral infections in an animal caused by Herpes Simplex Virus Types 1 and 2. Compositions are described for use in the treatment comprising purified nerve growth factor alone or in conjunction with a Herpes Simplex Viral antiviral agent.

L99 ANSWER 15 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998097042 EMBASE
TITLE: Comprehensive management of amyotrophic lateral sclerosis.
AUTHOR: Carter G.T.; Miller R.G.
CORPORATE SOURCE: Dr. G.T. Carter, 500 SE Washington, Chehalis, WA 98532, United States
SOURCE: Physical Medicine and Rehabilitation Clinics of North America, (1998) 9/1 (271-284).
Refs: 48
ISSN: 1047-9651 CODEN: PMRAFZ

COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Amyotrophic lateral sclerosis (ALS) is a rapidly progressive motor neuron disease that poses a myriad of clinical problems. Patients with ALS are best treated in a multidisciplinary setting involving physicians, clinical nursing specialists, and physical, occupational, speech, and respiratory therapists, as well as psychologists and social workers. Palliative and rehabilitative strategies may ease suffering, while new treatments provide hope for effective treatment of this disease.

L99 ANSWER 16 OF 16 EMBASE
on STN
ACCESSION NUMBER: 93307926 EMBASE
DOCUMENT NUMBER: 1993307926
TITLE: Treatment of Parkinson's disease.
AUTHOR: Calne D.B.
CORPORATE SOURCE: Department of Medicine, University of British Columbia, University Hospital,Vancouver, BC V6T 2B5, Canada
SOURCE: New England Journal of Medicine, (1993) 329/14 (1021-1027). ISSN: 0028-4793 CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

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=> fil medl; d que l20; d que l22
FILE 'MEDLINE' ENTERED AT 13:29:28 ON 20 AUG 2004

 FILE LAST UPDATED: 19 AUG 2004 (20040819/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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claim 1

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L1        17224 SEA FILE=MEDLINE ABB=ON  NERVE GROWTH FACTORS+NT/CT
L13       28447 SEA FILE=MEDLINE ABB=ON  ANXIETY+NT/CT
L14       32890 SEA FILE=MEDLINE ABB=ON  ANXIETY DISORDERS+NT/CT - includes panic attacks & agoraphobia
L15        2192 SEA FILE=MEDLINE ABB=ON  PANIC/CT
L16        8055 SEA FILE=MEDLINE ABB=ON  "ATTENTION DEFICIT DISORDER WITH
                HYPERACTIVITY"/CT
L17        2450 SEA FILE=MEDLINE ABB=ON  PREMENSTRUAL SYNDROME/CT
L18         258 SEA FILE=MEDLINE ABB=ON  PREMENSTRUAL(2A)DYSPHORIC(2A)DISORDER#

L19        7232 SEA FILE=MEDLINE ABB=ON  L1(L)(AD OR PD OR PK OR TU)/CT ---> AD - administration & dosage
L20           1 SEA FILE=MEDLINE ABB=ON  L19 AND (L13 OR L14 OR L15 OR L16 OR
                L17 OR L18)

                                          PD pharmacology
                                          PK - pharmacokinetics
                                          TU - therapeutic use

L1        17224 SEA FILE=MEDLINE ABB=ON  NERVE GROWTH FACTORS+NT/CT
L10       34580 SEA FILE=MEDLINE ABB=ON  DEPRESSION/CT
L11       44201 SEA FILE=MEDLINE ABB=ON  DEPRESSIVE DISORDER+NT/CT
L12       17430 SEA FILE=MEDLINE ABB=ON  BIPOLAR DISORDER+NT/CT
L19        7232 SEA FILE=MEDLINE ABB=ON  L1(L)(AD OR PD OR PK OR TU)/CT
L21       25534 SEA FILE=MEDLINE ABB=ON  (L10 OR L11 OR L12)(L)(DT OR PC)/CT
L22           7 SEA FILE=MEDLINE ABB=ON  L21 AND L19
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↳ DT - drug therapy
PC - prevention & control

```
=> s l20 or l22

L166          8 L20 OR L22

=> fil embase; d que l58; d que l60; d que l62; d que l63; d que l64

FILE 'EMBASE' ENTERED AT 13:29:29 ON 20 AUG 2004
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 FILE COVERS 1974 TO 19 Aug 2004 (20040819/ED)

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L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L33        6964 SEA FILE=EMBASE ABB=ON  L24(L)EC/CT - EC - endogenous compound
L38        2297 SEA FILE=EMBASE ABB=ON  AGORAPHOBIA/CT
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L40         167 SEA FILE=EMBASE ABB=ON  PREMENSTRUAL DYSPHORIC DISORDER/CT
L41        2309 SEA FILE=EMBASE ABB=ON  PREMENSTRUAL SYNDROME/CT
L58           0 SEA FILE=EMBASE ABB=ON  (L24 NOT L33) AND (L38 OR L40 OR L41)



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L36       36630 SEA FILE=EMBASE ABB=ON  ANXIETY/CT
L37       35723 SEA FILE=EMBASE ABB=ON  ANXIETY DISORDER+NT/CT
L39        7805 SEA FILE=EMBASE ABB=ON  ATTENTION DEFICIT DISORDER/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L60           5 SEA FILE=EMBASE ABB=ON  L49 AND (L36 OR L37 OR L39)(L)(DT OR
                PC)/CT

L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L35       97870 SEA FILE=EMBASE ABB=ON  DEPRESSION+NT/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L61       21588 SEA FILE=EMBASE ABB=ON  L35(L)(DT OR PC)/CT
L62          18 SEA FILE=EMBASE ABB=ON  L61 AND L49



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L35       97870 SEA FILE=EMBASE ABB=ON  DEPRESSION+NT/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L61       21588 SEA FILE=EMBASE ABB=ON  L35(L)(DT OR PC)/CT
L63           3 SEA FILE=EMBASE ABB=ON  L61 AND L49/MAJ



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L35       97870 SEA FILE=EMBASE ABB=ON  DEPRESSION+NT/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L61       21588 SEA FILE=EMBASE ABB=ON  L35(L)(DT OR PC)/CT
L64           4 SEA FILE=EMBASE ABB=ON  L61/MAJ AND L49


=> s l60 or l63 or l64

L167         12 L60 OR L63 OR L64

=> fil drugu; d que l115

FILE 'DRUGU' ENTERED AT 13:29:30 ON 20 AUG 2004
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FILE LAST UPDATED: 19 AUG 2004        <20040819/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<

>>>  A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED
     IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED
     ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
     STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
     EDITION).
     FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide
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AD - administration
DO - dosage
PD - pharmacology
PK - pharmacokinetics
DT - drug therapy
PC - prevention

L35 - includes Bi Polar disorder

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L100        690 SEA FILE=DRUGU ABB=ON  NERVE -GROWTH-FACTOR/CT OR NERVE-GROWTH
                -FACTOR/CT OR NERVE-GROWTH-FACTOR/CT
L101        106 SEA FILE=DRUGU ABB=ON  NEUROTROPHIC-FACTOR/CT OR NEUROTROPHIN?/
                CT
L102      14587 SEA FILE=DRUGU ABB=ON  DEPRESSION+NT/CT
L103        954 SEA FILE=DRUGU ABB=ON  BIPOLAR-DISORDER/CT OR BIPOLAR/CT
L104       5562 SEA FILE=DRUGU ABB=ON  ANXIETY/CT OR ANXIETY-DISORDER/CT
L105       1137 SEA FILE=DRUGU ABB=ON  PANIC/CT OR PANIC -DISORDER/CT OR
                PANIC-ATTACK/CT OR PANIC-DISORDER/CT
L106         46 SEA FILE=DRUGU ABB=ON  ATTENTION-DEFICIT-DISORDER/CT OR
                ATTENTION-DEFICIT-HYPERACT.DISORDER/CT OR ATTENTION-DEFICIT-HYP
                ERACTIVITY-DISORDER/CT OR ATTENTION-DEFICIT-HYPERKINETIC-DISORD
                ER/CT
L107         84 SEA FILE=DRUGU ABB=ON  PREMENSTRUAL/CT OR PREMENSTRUAL-DYSPHORI
                C-DISORDER/CT
L108        318 SEA FILE=DRUGU ABB=ON  PREMENSTRUAL-SYNDROME/CT OR PREMENSTRUAL
                -TENSION/CT
L115          0 SEA FILE=DRUGU ABB=ON  (L100 OR L101) AND (L102 OR L103 OR
                L104 OR L105 OR L106 OR L107 OR L108)


=> fil capl wpids; d que l158; d que l161

FILE 'CAPLUS' ENTERED AT 13:29:31 ON 20 AUG 2004
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L117      21524 SEA (NERVE OR NEURON?)(2A) (GROWTH FACTOR#) OR NEUROTROPHIC
                FACTOR# OR NEUREGULIN# OR NEUROTROPHIN# OR GLIAL MATURATION
                FACTOR#
L122       1761 SEA PREMENSTRUAL?
L150       1687 SEA L117(5A)(ADMIN? OR THERAP? OR PHARMAC? OR TREAT?)
L158          3 SEA L150 AND L122



L117      21524 SEA (NERVE OR NEURON?)(2A) (GROWTH FACTOR#) OR NEUROTROPHIC
                FACTOR# OR NEUREGULIN# OR NEUROTROPHIN# OR GLIAL MATURATION
                FACTOR#
L118      51989 SEA DEPRESSION OR DEPRESSIVE DISORDER#
L119      52444 SEA BIPOLAR OR BI POLAR OR MANI?(2A) DEPRESS?
L120      16388 SEA ANXIETY OR PANIC OR AGORAPHOBI?
L121       2925 SEA ATTENTION DEFICIT OR ADHD
L122       1761 SEA PREMENSTRUAL?
L141       2234 SEA L117(10A)(ADMIN? OR THERAP? OR PHARMAC? OR TREAT?)
L161         21 SEA L141 AND L118 AND (L119 OR L120 OR L121 OR L122)


=> s l158 or l161

L168         21 L158 OR L161

=> dup rem l166,l168,l167
FILE 'MEDLINE' ENTERED AT 13:30:00 ON 20 AUG 2004
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FILE 'CAPLUS' ENTERED AT 13:30:00 ON 20 AUG 2004
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PROCESSING COMPLETED FOR L166
PROCESSING COMPLETED FOR L168
PROCESSING COMPLETED FOR L167
L169         39 DUP REM L166 L168 L167 (2 DUPLICATES REMOVED)
                ANSWERS '1-8' FROM FILE MEDLINE
                ANSWERS '9-16' FROM FILE CAPLUS
                ANSWERS '17-27' FROM FILE WPIDS
                ANSWERS '28-39' FROM FILE EMBASE

=> d ibib ed ab l169 1-39

L169 ANSWER 1 OF 39     MEDLINE on STN
ACCESSION NUMBER:   2004246436     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15145621
TITLE:              Critical role of brain-derived neurotrophic factor in mood
                    disorders.
AUTHOR:             Hashimoto Kenji; Shimizu Eiji; Iyo Masaomi
CORPORATE SOURCE:   Department of Psychiatry, Chiba University Graduate School
                    of Medicine, 1-8-1 Inohana, Chiba 260-8670, Japan..
                    hashimoto@faculty.chiba-u.jp
SOURCE:             Brain research. Brain research reviews, (2004 May) 45 (2)
                    104-14.  Ref: 121
                    Journal code: 8908638. ISSN: 0165-0173.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200408
ENTRY DATE:         Entered STN: 20040518
                    Last Updated on STN: 20040819
                    Entered Medline: 20040818
ED   Entered STN: 20040518
     Last Updated on STN: 20040819
     Entered Medline: 20040818
AB   The purpose of this review is to integrate what is currently known about
     the role of brain-derived neurotrophic factor (BDNF) in the
     pathophysiology of mood disorders including major depressive disorder
     (MDD) and bipolar disorder (BD).  We reviewed the pre-clinical and
     clinical papers demonstrating that BDNF plays a role in the
     pathophysiology of mood disorders and in the mechanism of action of
     therapeutic agents.  Pre-clinical studies suggest that the expression of
     BDNF might be a downstream target of antidepressant treatments and mood
     stabilizers such as lithium and valproate, and that BDNF exerts
     antidepressant activity in animal models of depression.  Furthermore, BDNF
     protects against stress-induced neuronal damage, and it might affect
     neurogenesis in the hippocampus, which is thought to be involved in the
     pathogenesis of mood disorders.  Clinical studies have demonstrated that
     serum levels of BDNF in drug-naive patients with MDD are significantly
     decreased as compared with normal controls, and that BDNF might be an
     important agent for therapeutic recovery from MDD.  Moreover, recent
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findings from family-based association studies have suggested that the BDNF gene is a potential risk locus for the development of BD. These findings suggest that BDNF plays a critical role in the pathophysiology of mood disorders and in the activity of therapeutic agents in patients with mood disorders. New agents capable of enhancing BDNF levels may lead aid the development of novel therapeutic drugs for patients with mood disorders.

L169 ANSWER 2 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2004318139 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15219473
TITLE: Pramipexole for bipolar II depression: a placebo-controlled proof of concept study.
AUTHOR: Zarate Carlos A Jr; Payne Jennifer L; Singh Jaskaran; Quiroz Jorge A; Luckenbaugh David A; Denicoff Kirk D; Charney Dennis S; Manji Husseini K
CORPORATE SOURCE: Laboratory of Molecular Pathophysiology, Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institute of Health, Department of Human and Health Services, Bethesda, Maryland, USA.
SOURCE: Biological psychiatry, (2004 Jul 1) 56 (1) 54-60. Journal code: 0213264. ISSN: 0006-3223.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040629 Last Updated on STN: 20040806 Entered Medline: 20040805
ED Entered STN: 20040629
Last Updated on STN: 20040806
Entered Medline: 20040805
AB BACKGROUND: The original serotonergic and noradrenergic hypotheses do not fully account for the neurobiology of depression or mechanism of action of effective antidepressants. Research implicates a potential role of the dopaminergic system in the pathophysiology of bipolar disorder. The current study was undertaken as a proof of the concept that dopamine agonists will be effective in patients with bipolar II depression. METHODS: In a double-blind, placebo-controlled study, 21 patients with DSM-IV bipolar II disorder, depressive phase on therapeutic levels of lithium or valproate were randomly assigned to treatment with pramipexole (n = 10) or placebo (n = 11) for 6 weeks. Primary efficacy was assessed by the Montgomery-Asberg Depression Rating Scale. RESULTS: All subjects except for one in each group completed the study. The analysis of variance for total Montgomery-Asberg Depression Rating Scale scores showed a significant treatment effect. A therapeutic response (>50% decrease in Montgomery-Asberg Depression Rating Scale from baseline) occurred in 60% of patients taking pramipexole and 9% taking placebo (p =.02). One subject on pramipexole and two on placebo developed hypomanic symptoms. CONCLUSIONS: The dopamine agonist pramipexole was found to have significant antidepressant effects in patients with bipolar II depression.

L169 ANSWER 3 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2003355493 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12888182
TITLE: S100B and response to treatment in major depression: a pilot study.
AUTHOR: Arolt Volker; Peters Marion; Erfurth Andreas; Wiesmann

Martin; Missler Ulrich; Rudolf Sebastian; Kirchner Holger; Rothermundt Matthias
CORPORATE SOURCE: Department of Psychiatry, University of Muenster, Albert-Schweitzer-Strasse 11, D-48129 Muenster, Germany.. arolt@uni-muenster.de
SOURCE: European neuropsychopharmacology : journal of the European College of Neuropsychopharmacology, (2003 Aug) 13 (4) 235-9.
Journal code: 9111390. ISSN: 0924-977X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030731
Last Updated on STN: 20031004
Entered Medline: 20031003

ED Entered STN: 20030731
Last Updated on STN: 20031004
Entered Medline: 20031003

AB S100B is a protein which exerts both detrimental and neurotrophic effects, depending on its concentration in brain tissue. An increase of S100B in micromolar concentrations is observed in traumatic brain conditions and is associated with poor outcome. Micromolar levels of extracellular S100B in vitro may have deleterious effects. However, in nanomolar concentrations S100B has multiple neurotrophic effects in vitro may in vivo be regarded as a hallmark of neuroprotective efforts. This pilot study addresses the hypothesis that S100B serum concentrations may be of predictive validity for the response to antidepressant treatment in patients with major depression. S100B plasma levels were determined in 25 patients with major depression and 25 matched healthy controls using an immunofluorimetric sandwich assay. S100B plasma levels were significantly higher in major depressive patients than in healthy controls and positively correlated with treatment response after 4 weeks of treatment. In a linear regression model, a significant predictive effect was found only for S100B and severity of depressive symptoms upon admission. These results suggest that neuroprotective functions of S100B counterbalance neurodegenerative mechanisms that are involved in the pathophysiology of major depression and in the response to antidepressant treatment.

L169 ANSWER 4 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2002209806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11943826
TITLE: Brain-derived neurotrophic factor produces antidepressant effects in behavioral models of depression.
AUTHOR: Shirayama Yukihiko; Chen Andrew C-H; Nakagawa Shin; Russell David S; Duman Ronald S .
CORPORATE SOURCE: Division of Molecular Psychiatry, Abraham Ribicoff Research Facilities, Connecticut Mental Health Center, Yale University School of Medicine, New Haven, Connecticut 06508, USA.
CONTRACT NUMBER: 2PO1 MH25642 (NIMH)
MH45481 (NIMH)
SOURCE: Journal of neuroscience : official journal of the Society for Neuroscience, (2002 Apr 15) 22 (8) 3251-61.
Journal code: 8102140. ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020412
Last Updated on STN: 20020423
Entered Medline: 20020422

ED Entered STN: 20020412
Last Updated on STN: 20020423
Entered Medline: 20020422

AB Previous studies demonstrated that antidepressant treatment increases the expression of brain-derived neurotrophic factor (BDNF) in rat hippocampus. The present study was conducted to test the hypothesis that BDNF in the hippocampus produces an antidepressant effect in behavioral models of depression, the learned helplessness (LH) and forced swim test (FST) paradigms. A single bilateral infusion of BDNF into the dentate gyrus of hippocampus produced an antidepressant effect in both the LH and FST that was comparable in magnitude with repeated systemic administration of a chemical antidepressant. These effects were observed as early as 3 d after a single infusion of BDNF and lasted for at least 10 d. Similar effects were observed with neurotrophin-3 (NT-3) but not nerve growth factor. Infusions of BDNF and NT-3 did not influence locomotor activity or passive avoidance. The results provide further support for the hypothesis that BDNF contributes to the therapeutic action of antidepressant treatment.

L169 ANSWER 5 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2001050683 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11103878
TITLE: Studies in animal models and humans suggesting a role of nerve growth factor in schizophrenia-like disorders.
AUTHOR: Aloe L; Iannitelli A; Angelucci F; Bersani G; Fiore M
CORPORATE SOURCE: Institute of Neurobiology, CNR, Rome, Italy..
aloe@in.rm.cnr.it
SOURCE: Behavioural pharmacology, (2000 Jun) 11 (3-4) 235-42. Ref: 106
Journal code: 9013016. ISSN: 0955-8810.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001214

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001214

AB Neurotrophic factors, such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), are known to play a crucial role in growth, differentiation and function in a variety of brain neurons during development and in adult life. We have recently shown that environmental changes, aggressive behavior and anxiety-like responses alter both circulating and brain basal NGF levels. In the present review, we present data obtained using animal models which suggest that neurotrophic factors, particularly NGF and BDNF, might be implicated in mechanism(s) leading to a condition associated with schizophrenic-like behaviors. The hypothesis that neurotrophins of the NGF family can be implicated in some maldevelopmental aspects of schizophrenia is supported by findings indicating that the constitutive levels of NGF and BDNF are affected in schizophrenic patients.

L169 ANSWER 6 OF 39 MEDLINE on STN

ACCESSION NUMBER: 2000048344 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10581643
TITLE: Prevention of muscimol-induced long-term depression by brain-derived neurotrophic factor.
AUTHOR: Akhondzadeh S; Stone T
CORPORATE SOURCE: Institute of Medicinal Plants, Tehran, Iran.. s.akhond@neda.net
SOURCE: Progress in neuro-psychopharmacology & biological psychiatry, (1999 Oct) 23 (7) 1215-26. Journal code: 8211617. ISSN: 0278-5846.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991221

ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991221

AB 1. The authors have recently reported a new protocol for inducing long-term depression through activation of GABAA receptors in the hippocampal slices. This long-term depression is reversed by bicuculline and potentiated by neurosteroids such as alphaxalone. It was also shown that glutamate receptor activity is not involved in the induction of this novel type of long-term depression. Brain derived neurotrophic factor is a member of the neurotrophins family widely expressed in the central nervous system. There is increasing evidence that indicate an important role for brain-derived neurotrophic factor in synaptic plasticity. It has been reported that brain-derived neurotrophic factor level is downregulated by GABA system. The present study investigated a possible relation between muscimol-induced long-term depression and brain-derived neurotrophic factor level. 2. Extracellular recordings were made in the CA1 pyramidal cell layer of rat hippocampal slices following orthodromic stimulation of Schaffer collateral fibers in stratum radiatum. 3. It was observed that brain-derived neurotrophic factor at concentration that did not have any effect itself on the population spike, prevents the induction of long-term depression by muscimol. In addition to this, K-252a an inhibitor of Trk type kinase blocked the prevention of muscimol-induced LTD by brain-derived neurotrophic factor. 4. The results suggest that there is an interaction between muscimol-induced long-term depression and brain-derived neurotrophic factor and may explain the post receptor mechanism of muscimol-induced long-term depression through a bilateral relation between GABAA activity and brain-derived neurotrophic factor.

L169 ANSWER 7 OF 39 MEDLINE on STN
ACCESSION NUMBER: 1998334413 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9671338
TITLE: When neurotrophic factors get on your nerves: therapy for neurodegenerative disorders.
AUTHOR: Stahl S M
CORPORATE SOURCE: Clinical Neuroscience Research Center in San Diego and the Department of Psychiatry at the University of California San Diego, USA.
SOURCE: Journal of clinical psychiatry, (1998 Jun) 59 (6) 277-8. Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807

ENTRY DATE: Entered STN: 19980731
Last Updated on STN: 20000303
Entered Medline: 19980722
ED Entered STN: 19980731
Last Updated on STN: 20000303
Entered Medline: 19980722

L169 ANSWER 8 OF 39 MEDLINE on STN
ACCESSION NUMBER: 93120913 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1282410
TITLE: [Nerve growth factor and the state of serotoninergic system in endogenous depression and mental retardation]. Faktor rosta nervov i sostoianie serotoninergicheskoi sistemy pri endogennykh depressiiakh i zaderzhke umstvennogo razvitiia.
AUTHOR: Brusov O S; Lideman R R
SOURCE: Vestnik Rossiiskoi akademii meditsinskikh nauk / Rossiiskaia akademiia meditsinskikh nauk, (1992) (8) 16-21. Journal code: 9215641. ISSN: 0869-6047.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 20000303
Entered Medline: 19930211
ED Entered STN: 19930226
Last Updated on STN: 20000303
Entered Medline: 19930211
AB Platelet parameters of the serotonin system were studied in patients with endogenous depressions and children with late documented phenylketonuria (PKU) before and after antidepressive therapy. There was a significant decrease in the rate of back platelet uptake of 3H-serotonin and an increase in the sensitivity of serotonin receptors to serotonin in the patients before therapy and normalization of these parameters after therapy. The normalization correlated with clinical improvement in patients with endogenous depression. The course therapy with L-DOPA and the antidepressant azaphen resulted in a substantial mental improvement in children with PKU. There was a significant reduction in the ability of platelets from the patients in question to react by releasing 3H-serotonin in response to nerve growth factor stimulation of cells in vitro.

L169 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:430746 CAPLUS
DOCUMENT NUMBER: 140:400710
TITLE: Method of **treatment** of psychological conditions and associated symptoms with the **administration** of **nerve growth factor**
INVENTOR(S): McMichael, John; Unice, Kenneth A.
PATENT ASSIGNEE(S): Milkhaus Laboratory, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004043462 A1 20040527 WO 2003-US31380 20031003
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004127409 A1 20040701 US 2003-624328 20030722
PRIORITY APPLN. INFO.: US 2002-424443P P 20021107
US 2003-624328 A 20030722

ED Entered STN: 27 May 2004
AB Method for administering nerve growth factor to treat various psychol. conditions such as of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, and attention deficit syndrome, and alleviate symptoms assocd. with premenstrual syndrome (PMS), premenstrual dysphoric disorder (PMDD), sleep disorders, tension headaches, and constipation that arise as complications from a psychol. condition.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:162676 CAPLUS
DOCUMENT NUMBER: 140:199343
TITLE: Preparation of aminopyrimidine derivatives as protein kinase inhibitors
INVENTOR(S): Cochran, John; Green, Jeremy; Hale, Michael R.; Ledford, Brian; Maltais, Francois; Nanthakumar, Suganthini
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016597	A2	20040226	WO 2003-US25333	20030812
WO 2004016597	A3	20040422		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004106615 A1 20040603 US 2003-639784 20030812
PRIORITY APPLN. INFO.: US 2002-403256P P 20020814
US 2002-416802P P 20021008
OTHER SOURCE(S): MARPAT 140:199343
ED Entered STN: 29 Feb 2004
AB Title compds. I [wherein B = 6-membered aryl ring with 0-3 N atoms, Z1, Z2 = independently N, CH; T, Q = independently satd. or unsatd. alkylidene; U

= NH and derivs., NHCO2 and derivs., o, CONH and derivs., CO, CO2, OCO, NHSO2 and derivs., SO2NH and derivs., SO2, etc.; m, n = independently 0 or 1; p = 0-4; R1 = R or Ar; R = H, (un)substituted aliph. group; Ar = (un)substituted 6-10 membered aryl ring, 5-10 membered heteroaryl ring having 1-4 heteroatoms, or a 3-10 heterocyclyl membered ring having 1-4 heteroatoms; R3 = R, Ar, (CH2)yCH(R5)2 or CN; y = 0-6; R2 = (CH2)yCH(R5)2, (CH2)yCH(R4)CH(R5)2; R4 = R, (CH2)wOR, (CH2)wN(R)2 or (CH2)wSR; w = 0-4; R5 = independently Ar, OR, CO2R, SR, SO2R, CN, N(Ar)(R), (un)substituted aliph., etc.; R6 = independently R, F, Cl, NH2 and derivs., OR, SR, SO2R, NRSO2R, CN, SO2N(R)2, etc.; and their pharmaceutical acceptable salts] were prepd. as protein kinase inhibitors (no data). For example, II was prepd. in 3 steps by Pd-cross coupling of 2,4-dichloro-5-fluoropyrimidine with 4-methoxycarbonylphenyl boronic acid (III), acylation of (S)-3-chlorophenyl glycinol with III, and alkylation of isopropylamine with 2-chloropyrimidine intermediate. I and their formulations are useful for treating or lessening the severity of a variety of disorders, including stroke, inflammatory disorders, autoimmune diseases such as SLE lupus and psoriasis, proliferative disorders such as cancer, and conditions assocd. with organ transplantation (no data).

L169 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:467858 CAPLUS
DOCUMENT NUMBER: 141:38524
TITLE: Preparation of N-arylalkyl-3-aminoalkoxyindoles as 5-HT and/or melatonin receptor ligands for treatment of CNS disorders
INVENTOR(S): Ramakrishna, Venkata Satya Nirogi; Shirsath, Vikas Shreekrishna; Kambhampati, Rama Sastri; Rao, Venkata Satya Veerabhadra Vadlamudi; Jasti, Venkateswarlu
PATENT ASSIGNEE(S): Suven Life Sciences Limited, India
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048331	A1	20040610	WO 2003-IN371	20031125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2002-MA885 A 20021128
OTHER SOURCE(S): MARPAT 141:38524
ED Entered STN: 10 Jun 2004
AB Title compds. I [wherein R1-R12 = independently H, halo, perhaloalkyl, OH, SH, NH2, NO2, CN, CHO, C(=NH)NH2, guanidino, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, alkoxy, (hetero)aryl(oxy), heterocyclyl(oxy), acyl(oxy), acylamino, carboxy esters, hydrazino, sulfonic acids, phosphoric acids, etc.; or 2 adjacent R-groups together with the C's to which they are attached may form a 5-6 membered (hetero)cycle; or CR11R12 = (hetero)cycle; R13 and R14 = independently H, (ar)alkyl, aryl; or NR13R14 = heterocyclyl; A = 1-2 H, O, OH, alkoxy; n = 1-8, preferably 1-4;

with provisos; and stereoisomers, radioisotopes, geometric forms, N-oxides, polymorphs, pharmaceutically acceptable salts, pharmaceutically acceptable solvates, useful bioactive metabolites, prodrugs, and any suitable combination of the above] were prepd. as serotonin (5-HT) and/or melatonin receptor modulators (no data). Further described are various methods of administering I, i.e. pharmaceutically acceptable dosage forms, their compn., and their use in either therapy or diagnosis. I and their pharmaceutical compns. are expected to be useful for the treatment of various CNS disorders (no data). For example, [2-[(1H-indol-3-yl)oxy]ethyl]dimethylamine was benzylated using NaH and PhCH2Br in DMF to give II.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:467855 CAPLUS
DOCUMENT NUMBER: 141:23419
TITLE: Preparation of N-arylsulfonyl-3-aminoalkoxyindoles as 5-HT and/or melatonin receptor modulators
INVENTOR(S): Ramakrishna, Venkata Satya Nirogi; Shirsath, Vikas Shreekrishna; Kambhampati, Rama Sastri; Rao, Venkata Satya Veerabhadra Vadlamudi; Jasti, Venkateswarlu
PATENT ASSIGNEE(S): Suven Life Sciences Limited, India
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048328	A2	20040610	WO 2003-IN370	20031125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2002-MA883 A 20021128
OTHER SOURCE(S): MARPAT 141:23419
ED Entered STN: 10 Jun 2004
AB Title compds. I [wherein X = (CR11R12)n; n = 1-8; R1-R12 = independently H, halo, perhaloalkyl, OH, SH, NO2, CN, CHO, amidino, guanidino, (un)substituted cyclo/bicyclo/ar/heterocyclyl/amino/thio/alkoxy/alkyl, cyclo/bicycloalkenyl, alkynyl, aryloxy, hetero/aryl, acyl/monoalkyl/dialkyl/aryl/diaryl/aralkyl/alkoxycarbonyl/amino, alkoxycarbonyl, alkylamidino, alkylguanidino, hydrazino, hydroxylamino, CO2H and derivs., SO3H and derivs.; R1CCR2, R2CCR3, R3CCR4, R5CCR6, R6CCR7, R7CCR8, R8CCR9 = 5- or 6-membered ring; R11CCR12 = 3-6 membered ring; R13, R14 = H, ar/alkyl, aryl or R13NR14 = 3-7 membered ring; their stereoisomers, radioisotopes, geometric forms, N-oxides, polymorphs, pharmaceutically acceptable salts and solvates, their useful bio-active metabolites and any suitable combination of the above] were prepd. as 5-HT and/or melatonin receptor modulators (no data). For example, II was prepd. by reacting N-[2-(1H-indol-3-yloxy)ethyl]dimethylamine with 4-bromobenzenesulfonyl chloride in DMF in the presence of NaH. Ten biol.

assays are given (no data). I are 5-HT ligands e.g. agonists or antagonists (no data). I are melatonergic ligands, e.g. agonists and antagonists, or they interact with both 5-HT and/or Melatonin receptors (no data).

L169 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:796724 CAPLUS
DOCUMENT NUMBER: 139:286374
TITLE: Theraputic methods and uses of sapogenins and their derivatives
INVENTOR(S): Rees, Daryl; Gunning, Phil; Orsi, Antonia; Xia, Zongqin; Hu, Yaer
PATENT ASSIGNEE(S): Phytopharm PLC, UK
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082893	A2	20031009	WO 2003-GB1380	20030327
WO 2003082893	C1	20031231		
WO 2003082893	A3	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002079221	A2	20021010	WO 2002-GB1578	20020328
WO 2002079221	A3	20030417		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
AR 2002-101170	A	20020327
US 2002-368178P	P	20020328
WO 2002-GB1578	A	20020328
GB 2001-7822	A	20010328

OTHER SOURCE(S): MARPAT 139:286374
ED Entered STN: 10 Oct 2003
AB The invention discloses therapeutic methods and uses of certain steroidal sapogenins (Markush structures included), related compds. and derivs. thereof, in the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment.

L169 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:5934 CAPLUS
DOCUMENT NUMBER: 138:73272
TITLE: Preparation of piperazinylpyrimidines as 5-HT2 receptor ligands for treatment of sexual disorders
INVENTOR(S): Chiang, Yuan-ching Phoebe; Novomisle, William Albert; Welch, Willard Mckowan
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000663	A1	20030103	WO 2002-IB2261	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003105106	A1	20030605	US 2002-156884	20020528
US 2003125334	A1	20030703	US 2002-163881	20020605
NZ 529542	A	20031219	NZ 2002-529542	20020617
NZ 529543	A	20031219	NZ 2002-529543	20020617
EP 1401819	A1	20040331	EP 2002-735853	20020617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010503	A	20040518	BR 2002-10503	20020617
EE 200400025	A	20040615	EE 2004-25	20020617
PRIORITY APPLN. INFO.:			US 2001-299953P P	20010621
			WO 2002-IB2261 W	20020617

OTHER SOURCE(S): MARPAT 138:73272
ED Entered STN: 05 Jan 2003
AB Title compds. (I) [wherein X and Y = CR and Z = N; or Y and Z = CR and X = N; R = H, halo, alkyl(amino), or amino; W = O, S, NH, alkylamino, or acetylamino; at least one of R1, R5, R6, or R7 = independently halo, NO2, (alkyl)amino, CN, CONH2, (halo)alkyl, or alkoxy; or C2R1R5 = 5- or 6-membered arom. or fused ring; or R1 taken together with R2 or R8 forms a 5- or 6-membered fused ring; R2 and R8 = independently H or (cyclo)alkyl; n = 0-2; R3 and R9 = independently H, halo, alkyl, or alkyl substituted with OH, F, or alkoxy; R4 = H, OH, (hydroxy)alkyl, cyanoalkyl, alkylcarbonyl, alkoxy(carbonyl), or alkenyl; or N-oxides, prodrugs, pharmaceutically acceptable salts, solvates, or hydrates thereof] were prepd. as 5-hydroxytryptamine (5-HT) receptor ligands, in particular 5-HT2C receptor ligands. For example, 2,4-dichloropyrimidine was coupled with piperazine-1-carboxylic acid tert-Bu ester using Na2CO3 in EtOH to give 4-(2-chloropyrimidin-4-yl)piperazine-1-carboxylic acid tert-Bu ester. Substitution with 3,5-difluorobenzyl alc. using NaH in THF afforded 4-[2-(3,5-difluorobenzyloxy)pyrimidin-4-yl]piperazine-1-carboxylic acid tert-Bu ester. Deesterification followed by conversion to the salt produced II.bul.xHCl. Compds. of the invention demonstrated affinity at the serotonin 5HT2A and 5HT2C binding sites with Ki values ranging from 0.5 nM to 625 nM and 0.2 nM to 238 nM, resp. In functional assays, II acted as a partial agonist using 5-HT2A and 5-HT2C expressed NIH 3T3 cells with EC50 values in the range of 0.16 .mu.M to 7.6 .mu.M and 0.016 .mu.M

to 7.0 .mu.M, resp. I and pharmaceutical compns. contg. I are useful for the treatment of diseases linked to the activation of 5-HT2 receptors, such as sexual dysfunction (no data).
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:118697 CAPLUS
DOCUMENT NUMBER: 138:158859
TITLE: Nasal delivery of pharmaceutical compositions in powder form
INVENTOR(S): Moonga, Gursharan
PATENT ASSIGNEE(S): UK
SOURCE: Brit. UK Pat. Appl., 6 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2378383	A1	20030212	GB 2001-13725	20010606

PRIORITY APPLN. INFO.: GB 2001-13725 20010606
ED Entered STN: 14 Feb 2003
AB The invention relates to methods of prepn. of vaccines and pharmaceutical compns. for Nasal delivery. The nasal method of delivery of medicaments comprises new ways of treatment of individuals. The objective of the invention is to develop needle free drug delivery systems to facilitate faster delivery to the target in lower dosage. The introduction of the medicament in powder form in the nose by relative ease is attractive method in terms of patient compliance the other aspect of the invention relates to the Nasal delivery of pharmaceutical compns. of neurol. agents by means of olfactory neutral pathways. Theses agents included naturally occurring nerve growth promoting factors including phosphatidyl serine, insulin and insulinlike growth factors.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:234994 CAPLUS
DOCUMENT NUMBER: 122:1098
TITLE: Method of **treating depression** using **neurotrophins**
INVENTOR(S): Siuciak, Judith
PATENT ASSIGNEE(S): Regeneron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9423736	A1	19941027	WO 1994-US4047	19940414
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9467033	A1	19941108	AU 1994-67033	19940414

US 5599560 A 19970204 US 1994-337321 19941110
PRIORITY APPLN. INFO.: US 1993-47819 19930415
WO 1994-US4047 19940414

ED Entered STN: 10 Dec 1994
AB Intracranial or intrathecal infusion of neurotrophins, preferably brain-derived neurotrophic factor, is used for the alleviation of symptoms of depression, as demonstrated by redn. of despair in the animal forced swim test. Alterations in serotonin levels brought about by neurotrophins suggested use of these factors for the treatment of other disorders caused by defects in serotonin activity.

L169 ANSWER 17 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-534112 [51] WPIDS
DOC. NO. CPI: C2004-196477
TITLE: New (1,2,4)triazolo(4,3-b)pyridazine compounds useful for the treatment of e.g. proliferative disorder, cardiac disorder, neurodegenerative disorder comprises (1,2,4)triazolo(4,3-b)pyridazine compounds.
DERWENT CLASS: B02
INVENTOR(S): GREEN, J; GREY, R; PIERCE, A C
PATENT ASSIGNEE(S): (VERT-N) VERTEX PHARM INC
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004058769	A2	20040715	(200451)*	EN	89

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004058769	A2	WO 2003-US39990	20031217

PRIORITY APPLN. INFO: US 2002-435124P 20021218
ED 20040810
AB WO2004058769 A UPAB: 20040810
NOVELTY - New (1,2,4)triazolo(4,3-b)pyridazine compounds and their salts .
DETAILED DESCRIPTION - New (1,2,4)triazolo(4,3-b)pyridazine compounds of formula (I) and their salts.
R1 = OR3, SR3, or NR3R4;
R3 and R4 = (U')mR';
U' = optionally substituted 1-6C alkylidene chain (in which up to two methylene units of the chain are optionally replaced by -C(O)-, -C(O)C(O)-, -CONR-, -CONRNR-, -CO2-, -OC(O)-, -NRCO2-, -O-, -NRCONR-, -OC(O)NR-, -NRNR, -NRCO-, -S-, -SO-, -SO2-, -NR-, -SO2NR- or -NRSO2;
m = 0 or 1;
NR3+R4 = optionally substituted 5- - 8-membered heterocyclyl or heteroaryl ring having 1 - 3 heteroatoms of N, O or S;
R = H or optionally substituted 1-6C aliphatic group;
R' = H or optionally substituted group selected from 1-8C aliphatic, 6-10C aryl, or heteroaryl ring having 5 - 10 ring atoms or heterocyclyl ring having 3 - 10 ring atoms;
R+R' and R'+R' on the same substituent or different substituents = 5- - 8-membered heterocyclyl or heteroaryl ring having 1 - 3 heteroatoms

of N, O or S;
R2 = -(T)nAr1;
T = NR;
n = 0 or 1;
Ar1 = 3- - 7-membered saturated, partially unsaturated or fully unsaturated monocyclic ring (having 0 - 3 heteroatoms selected from N, O or S) or 8 - 10-membered saturated, partially unsaturated or fully unsaturated bicyclic ring system (having 0 - 5 heteroatoms selected from N, O or S).

Provided that (I) is not butanoic acid 2-(benzylamino)-3-((3-phenyl-1,2,4-triazolo (4,3-b)pyridazin-6-yl)hydrazono)-methyl ester, benzamide, N-(2,5-dihydro-3-methyl-5-oxo-1-(3-phenyl-1,2,4-triazolo(4,3-b)pyridazin-6-yl)-1H-pyrazol-4-yl or 2-propenoic acid, 2-(benzylamino)-3-(3,5-dimethyl-1-(3-phenyl-1,2,4-triazolo(4,3-b)pyridazin-6-yl)-1H-pyrazol-4-yl

An INDEPENDENT CLAIM is also included for:

(1) treating or lessening the severity of a disease or condition selected from proliferative disorder, cardiac disorder, neurodegenerative disorder, autoimmune disorder, a condition associated with organ transplant, anti-inflammatory disorder, an immunologically mediated disorder, a viral disease or a bone disorder involving administering the composition or (I); and

(2) a composition comprising compounds of (I), and a carrier, adjuvant or vehicle.

Provided that:

(a) when R2 is optionally substituted 1,3,5-triazine, then R1 is not N-morpholino;

(b) when R2 is nitro substituted pyrazolyl, furyl or thiophene, then R1 is not NR3R4;

(c) when R2 is furyl, then R2 is not NH2;

(d) when R2 is optionally substituted pyridyl or phenyl, then R1 is not OR3 where R3 is halogen substituted alkyl;

(e) when R2 is phenyl substituted with haloalkyl or haloalkoxy, then R1 is not NH(1-4C alkyl) or O(CH2)nN(Me)2;

(f) when R2 is phenyl substituted by OMe, Me, NO2, Cl or CF3, then R1 is not optionally substituted morpholino or piperazinyl;

(g) when R2 is phenyl or fluoro-substituted phenyl, R1 is not -O-CH2-(triazolyl);

(h) when R1 is -NH(cyclopropyl), then R2 is not phenyl substituted by CF3 in the para position; when R2 is unsubstituted phenyl, then R1 is not NH(CH)=NOH.

ACTIVITY - Cardiant; Cytostatic; Neuroprotective; Nootropic; Immunosuppressive; Antiinflammatory; Virucide; Osteopathic; Antiasthmatic; Antiallergic; Vasotropic; Antiangiogenic; Nephrotropic; Anti-HIV; Antipsoriatic; Antiarteriosclerotic; Endocrine-Gen.; Antiarthritic; Antirheumatic; Anticonvulsant; Antiparkinsonian; Hepatotropic; Cerebroprotective; Neuroleptic; Antidepressant; Tranquilizer; Cardiovascular-Gen.; Antidiabetic.

MECHANISM OF ACTION - PIM-1, glycogen synthase kinase (GSK)-3, cyclin dependent kinase (CDK)-2 or SRC kinase activity inhibitor. Cyclopropyl-(3-(3-fluoro-phenyl)-(1,2,4)triazolo(4,3-b)pyridazin-6-yl)-amine (A) was tested for their ability to inhibit PIM-1 using a standard coupled enzyme assay as given in Fox et al (1998) Protein Sci 7,2249 and showed IC50 value of less than 1 micro M.

USE - For treating or lessening the severity of a disease or condition e.g. proliferative disorder, cardiac disorder, neurodegenerative disorder, autoimmune disorder, a condition associated with organ transplant, inflammatory disorder, an immunologically mediated disorder, a viral disease or a bone disorder (claimed). Also in the treatment of e.g. cancer; inflammatory disease e.g. asthma, allergy, Crohn's disease and immunosuppression including transplantation rejection and autoimmune disease; Alzheimer's disease; restenosis; angiogenesis; glomerulonephritis; cytomegalovirus; HIV; herpes; psoriasis;

atherosclerosis; alopecia; rheumatoid arthritis; viral infections; neurodegenerative disorder; disorders associated with thymocyte apoptosis or proliferative disorder resulting from deregulation of the cell cycle; Huntington's disease, Parkinson's disease, basal ganglia movement disorder, chorea, dystonia, Wilson's disease, Pick disease, frontal lobe degeneration, progressive supranuclear palsy (PSP), Creutzfeldt-Jakob disease, taupathology and corticobasal degeneration (CBD), psychotic disorder (e.g. schizophrenia, AIDS-associated dementia, depression, bipolar disorder and anxiety disorder), cardiovascular disease, diabetes, amyotrophic lateral sclerosis (Lou Gehrig's disease), multiple sclerosis, cardiomyocytes hypertrophy, reperfusion/ischemia, stroke and baldness and bone remodeling disease e.g. osteoporosis and hepatitis B infection. For coating an implantable device such as prostheses; artificial valves; vascular grafts; stents and catheters.

ADVANTAGE - The compounds are inhibitors of protein kinases e.g. PIM-1; GSK-3; CDK-2 or SRC mammalian protein kinases. The compound enhances glycogen synthesis and/or lowers blood levels of glucose; inhibits the production of hyperphosphorylated Tau protein or beta -catenin.

Dwg.0/0

L169 ANSWER 18 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-500263 [47] WPIDS
DOC. NO. CPI: C2004-185294
TITLE: Modulating the activity of a (pro-)**neurotrophin** in a cell or an organism, useful for **treating** e.g. inflammatory disorders, comprises **administering** an agent that inhibits binding of (pro-)**neurotrophin** with Vps1 Op-domain receptor.
DERWENT CLASS: B04 D16
INVENTOR(S): NYKJAER, A; PETERSEN, C M
PATENT ASSIGNEE(S): (UYAA-N) UNIV AARHUS
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004056385	A2	20040708	(200447)*	EN	66

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004056385	A2	WO 2003-DK919	20031219

PRIORITY APPLN. INFO: DK 2002-1977 20021220
ED 20040723
AB WO2004056385 A UPAB: 20040723
NOVELTY - Modulating the activity of at least one neurotrophin and/or a pro-neurotrophin in a cell or an organism, such as an animal, comprising administering an agent capable of:

(a) binding to a receptor of the Vps1 Op-domain receptor family; and/or

(b) interfering with binding between a receptor of the Vps1 Op-domain receptor family and a neurotrophin and/or proneurotrophin; and/or

(c) modulating the expression of a receptor of the Vps1 Op-domain receptor family, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an in vitro method for screening for a compound which alters the binding of at least one neurotrophin and/or a pro-neurotrophin to a receptor of the Vps1 Op-domain receptor family;

(2) determining the effect of an agent on activity of neurotrophins and/or pro-neurotrophins in cells expressing a receptor of the Vps1 Op-domain receptor family;

(3) an agent capable of modulating the activity of at least one neurotrophin and/or a pro-neurotrophin when the neurotrophin and/or pro-neurotrophin binds to a receptor of the Vps1 Op-domain receptor family;

(4) modulating the transport of at least one neurotrophin and/or pro-neurotrophin out of, into or within a cell line or a cell expressing a receptor of the Vps1 Op-domain receptor family in an animal by administering an agent capable of binding a receptor of the Vps1 Op-domain receptor family;

(5) isolating a compound capable of altering the binding of at least one neurotrophin and/or proneurotrophin to a receptor of the Vps1 Op-domain receptor family;

(6) producing a pharmaceutical composition comprising performing the method of (5), and formulating the refined compound/-compound with reduced toxicity with a pharmaceutical carrier or diluent;

(7) a soluble receptor of the Vps1 Op-domain receptor family, its fragment or variant; and

(8) a pharmaceutical composition comprising a soluble receptor of the Vps1 Op-domain receptor family, its fragment or variant.

ACTIVITY - Antiinflammatory; Nephrotropic; Cardiovascular; Cytostatic; Neuroprotective; Nootropic; Antiparkinsonian; Cerebroprotective; Neuroleptic; Neuroleptic; Antidepressant; Antimanic.

No biological data given.

MECHANISM OF ACTION - Neurotropin Modulator; Proneutrophic Modulator.

USE - The soluble receptor is useful in the preparation of a medicament or a diagnostic agent for diagnosing neurotrophin and/or pro-**neurotrophin** related diseases. The agent is useful for **treating** a disease or disorder including inflammatory pain, diseases or disorders of pancreas, kidney disorders, lung disorders, cardiovascular disorders, various types of tumors, psychiatric disorders or neuronal disorders, Alzheimer's disease, Parkinson's disease, Huntington's chorea, stroke, ALS, peripheral neuropathies, necrosis or loss of neurons, nerve damage to trauma, kidney dysfunction, injury, and the toxic effects of chemotherapeutics used to treat cancer and AIDS, aberrant sprouting in epilepsy, schizophrenia, pancreas or lung injury and/or dysfunction, injury and/or dysfunction of the central and/or peripheral nervous systems, peripheral neuropathy, distal sensorimotor neuropathy, or autonomic neuropathies, such as reduced motility of the gastrointestinal tract or atony of the urinary bladder, post-polio syndrome or AIDS-associated neuropathy; hereditary neuropathies, such as Charcot-Marie-Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, Fabry's disease, and Dejerine-Sottas syndrome, **depression**, **mania** or Down's syndrome.

Dwg.0/7

L169 ANSWER 19 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-191352 [18] WPIDS
DOC. NO. CPI: C2004-075554
TITLE: New pyrazole derivatives are glycogen synthase kinase-3 inhibitors useful to treat spinal cord injury, glaucoma,

psychiatric disorder and asthma.
DERWENT CLASS: B02
INVENTOR(S): FORSTER, C J; PARK, L C; WANNAMAKER, M W; YAO, Y M; YAO, Y
PATENT ASSIGNEE(S): (FORS-I) FORSTER C J; (PARK-I) PARK L C; (WANN-I) WANNAMAKER M W; (YAOY-I) YAO Y M; (VERT-N) VERTEX PHARM INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004013140	A1	20040212	(200418)*	EN	65
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2004039007	A1	20040226	(200418)		
AU 2003257078	A1	20040223	(200453)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004013140	A1	WO 2003-US23950	20030731
US 2004039007	A1 Provisional	US 2002-400967P	20020802
		US 2003-632340	20030801
AU 2003257078	A1	AU 2003-257078	20030731

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003257078	A1 Based on	WO 2004013140

PRIORITY APPLN. INFO: US 2002-400967P 20020802; US 2003-632340 20030801
ED 20040316
AB WO2004013140 A UPAB: 20040316
NOVELTY - Pyrazole derivatives and their salts are new.
DETAILED DESCRIPTION - Pyrazole derivatives of formula (I) and their salts are new.
W = N or CH;
R1 = H or fluorine;
R-y = 1-4C aliphatic group, optionally substituted with N(R2)2 or a 5-6 membered saturated ring having 1-2 heteroatoms of N, O or S;
R2 = H or a 1-3C aliphatic optionally substituted with OH, N(R3)2 or a 5-6 membered saturated ring having 1-2 of N, O or S; and
R3 = H or a 1-3C aliphatic.
ACTIVITY - Immunosuppressive; Antiinflammatory; Neuroprotective; Vulnerary; Ophthalmological; Endocrine-Gen.; Cardiovascular-Gen.; Antiallergic; Antiasthmatic; Anticonvulsant; Nootropic; Antiparkinsonian; Anti-HIV; Cerebroprotective; Antidepressant; Tranquilizer; Hypnotic; Vasotropic; Angiogenesis-Inhibitor; Angiogenesis Stimulator; Cardiant; Neuroleptic; Antiinfertility.
MECHANISM OF ACTION - Glycogen synthase kinase-3 (GSK-3) inhibitor. (I) were tested for their ability to inhibit GSK-3 beta activity using a standard coupled enzyme system. The results showed that the inhibitory constant (Ki) of (I) was less than 100 micro M.
USE - (I) are used to treat autoimmune disease, inflammatory disease,

metabolic disorder, psychiatric disorder, diabetes, angiogenic disorder, tauopathy, a neurological or neurodegenerative disorder, a spinal cord injury, glaucoma, baldness and cardiovascular disease (preferably allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), multiple sclerosis (MS), an injury due to head trauma, schizophrenia, **anxiety**, **bipolar** disorder, tauopathy, a spinal cord or peripheral nerve injury, myocardial infarction, cardiomyocyte hypertrophy, glaucoma, **attention deficit** disorder (ADD), **depression**, a sleep disorder, reperfusion/ischemia, stroke and an angiogenic disorder, (particularly stroke, Alzheimer's disease and neurodegenerative disorder)). (I) are also used to decrease the sperm motility, inhibits glycogen synthase kinase-3 (GSK-3) activity in biological samples. (All claimed.)

ADVANTAGE - (I) are potent glycogen synthase kinase-3 inhibitors.

Dwg.0/2

L169 ANSWER 20 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-204833 [20] WPIDS
DOC. NO. CPI: C2004-080953
TITLE: New pyrazolo-(1,5-a)-1,3,5-triazoles and analogs, are endogenous **neurotrophic factor** synthesis and/or release promoters useful for **treating** diseases involving neuronal degeneration, e.g. Alzheimer's disease.
DERWENT CLASS: B02
INVENTOR(S): BERNARD, P; RABOISSON, P; JOSEPH, B
PATENT ASSIGNEE(S): (GREE-N) GREENPHARMA; (GREE-N) GREENPHARMA SA
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2842809	A1	20040130	(200420)*		52
WO 2004011464	A2	20040205	(200420)	FR	
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW				
AU 2003273473	A1	20040216	(200453)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2842809	A1	FR 2002-9519	20020726
WO 2004011464	A2	WO 2003-FR2354	20030725
AU 2003273473	A1	AU 2003-273473	20030725

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003273473	A1 Based on	WO 2004011464

PRIORITY APPLN. INFO: FR 2002-9519 20020726
ED 20040324
AB FR 2842809 A UPAB: 20040324
NOVELTY - Fused bicyclic azine compounds (I) (specifically

pyrazolo-(1,5-a)-1,3,5-triazoles) are new.

DETAILED DESCRIPTION - Fused bicyclic azine compounds of formula (I) and their tautomers, prodrugs, bio-precursors and acid or base addition salts are new.

A, B, D = C or N, provided that A and B are not both N;

R1 = H, 1-12C alkyl, cycloalkyl, aryl, aryl-(1-4C) alkyl, (1-12C) alkyl-aryl, 5-18C aromatic or non-aromatic heterocycle or NR'R'' or NHCOR';

R', R'' = H, alkyl, cycloalkyl, 6-12C aryl or 5-12C aromatic or non-aromatic heterocycle;

R2, R3 = H, halo, NO2, alkyl, carboxyalkyl (optionally as sodium salt), trifluoroalkyl, cycloalkyl, acyl, 2-6C alkenyl, 2-6C alkynyl, aryl, carboxyaryl (optionally as sodium salt), aryl-(1-4C) alkyl, alkylaryl, 5-12C heteroaryl, -CH(OH)-aryl, -CO-aryl, (CH2)n-CONH-(CH2)m-aryl, (CH2)n-SO2NH-(CH2)m-aryl, (CH2)n-CONH-CH(COOH)-(CH2)p-aryl, ORx, SRx or NRxRy;

n = 1-4;

m = 0-3;

p = 0-2;

Rx, Ry = H, alkyl, cycloalkyl, aryl, aryl-(1-4C) alkyl, (1-12C) alkyl-aryl, 5-12C aromatic or non-aromatic heterocycle, NR'R'' or NHCOR'; or

Rx+Ry = 2-6C linear or branched hydrocarbyl chain, optionally containing one or more double bonds and/or interrupted by O, S or N;

R5 = H, alkyl, cycloalkyl, 6-12C aryl or 5-12C heteroaryl;

R6+R7 = group completing a 5-6 membered ring (optionally containing another N, O or S heteroatom);

X = O, S or NRx; and

Y = halo, alkyl, 2-6C alkenyl, 2-6C alkynyl, phenyl, ORx, SRx or NRxRy;

provided that:

(i) unless specified otherwise alkyl moieties have 1-6C, cycloalkyl moieties have 3-6C, aryl moieties 6-18C and heterocycles contain 1-3 heteroatoms;

(ii) if the bond between N1 and C6 is single, then the bond between C6 and R8 is double and R8 = X;

(iii) if the bond between N1 and C6 is double, then the bond between C6 and R8 is single, R8 = Y and R1 is absent;

(iv) if the bond between A and B is single, then the bond between A and R2 is double and R2 = X;

(v) if the bond between A and B is double, then the bond between A and R2 is single and R5 is absent;

(vi) if the bond between C4 and D is single, then the bond between C4 and C7 is double; and

(vii) if the bond between C4 and D is double, then the bond between C4 and C7 is double and D is C or N with R5 absent.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Neuroprotective; Nootropic; Antidiabetic; Anticonvulsant; Antiparkinsonian; Ophthalmological; Vulnerary; Antiinflammatory; Immunomodulator; Antibacterial; Virucide; Cardiant; Anti-HIV; Antidepressant; Neuroleptic; Tranquilizer; Analgesic.

In tests in cultured fetal rat cerebral cortex neurones, sodium 4-((1-oxo-3-(4-oxo-pyrazolo-(1,5-a)-1,3,5-triazin-8-yl)-propyl)-amino)-benzoate (Ia) at 50 micro M significantly increased neuronal development (i.e. length and thickness).

MECHANISM OF ACTION - Endogenous neurotrophic factor synthesis and/or release promoter; carbon monoxide-dependent guanylate cyclase modulator; phosphodiesterase (PDE) inhibitor.

Typically (I) induce one or more of nerve growth factor (NGF), neurotrophic factor-3 (NT-3), brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNGF) and/or protein S-100 beta , due to increased intracellular cyclic guanosine monophosphate (cGMP) levels

caused by carbon monoxide-dependent guanylate cyclase modulation and/or PDE inhibition. Some PDE IV inhibiting compounds (I) also inhibit production of tumor necrosis factor alpha (TNF- alpha) by pro-inflammatory cells.

USE - Compounds (I) are used for treating diseases involving neuronal degeneration (claimed), e.g. age-associated cognitive disorders, Alzheimer's disease, neural lesions, peripheral neuropathy (including neuropathy caused by drugs such as oncolytic agents or associated with diabetes), Down's syndrome, cerebrovascular accidents, spasm-associated disorders (such as epilepsy), Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, Huntington's disease, retinopathy (especially pigmentary retinitis), trauma (e.g. accidents affecting the spinal column or compression of the optical nerve following glaucoma), chemical-induced neuronal disorders or secondary neurological disorders. More generally (I) show antiinflammatory, immunomodulatory, neurological, antimicrobial, antiviral and cardiovascular activities and are useful e.g. for treating (in addition to Alzheimer's disease, Parkinson's disease and age-associated memory loss) AIDS, diabetes, **depression**, schizophrenia, **bipolar** disorder, **attention deficit** disorder, fibromyalgia, dementia (such as Lewy body dementia) or **anxiety**.

Dwg.0/1

L169 ANSWER 21 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-863951 [80] WPIDS
DOC. NO. CPI: C2003-244196
TITLE: Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition by an ocular route of drug delivery.
DERWENT CLASS: A96 B05 B07 D22
INVENTOR(S): ABDULRAZIK, M
PATENT ASSIGNEE(S): (ABDU-I) ABDULRAZIK M
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003181354	A1	20030925	(200380)*		17

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003181354	A1	US 2003-354173	20030130

PRIORITY APPLN. INFO: IL 2002-147921 20020131
ED 20031211
AB US2003181354 A UPAB: 20031211
NOVELTY - Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition (A) by an ocular route of drug delivery.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for method (M) for the treatment of migraines in humans involving:

(a) administering a pharmaceutical composition (A') by an ocular route of drug delivery; or

(b) administering an established anti-migraine therapeutic agent by an ocular route of drug delivery.

ACTIVITY - CNS-Gen.; Vasotropic; Tranquilizer; Analgesic; Antimigraine; Neuroprotective; Anticonvulsant; Antiparkinsonian; Nootropic; Muscular-Gen.; Cytostatic; Antibacterial; Antiinflammatory;

Antidepressant; Neuroleptic; Antiaddictive; Eating-disorder-Gen.; Anorectic; Hypotensive; Auditory; Ophthalmological; Antiangiogenic; Cerebroprotective; Immunosuppressive; Antiarthritic; Antiarteriosclerotic; Anabolic; Immunomodulator; Uropathic; Sedative; Endocrine-Gen.; Hypnotic; Antimicrobial; Antialcoholic; Antismoking.

A 48-year old female patient with a history of migraine, and right eye primary open angle glaucoma was prescribed with brimonidine tartrate (0.2%) as a second topical antiglaucoma agent. The patient reported a substantial relief of migraine related symptoms.

MECHANISM OF ACTION - None given.

USE - For the treatment and/or prevention of central nervous system disorders and/or states in human or animal e.g. central nervous system ischemia, central nervous system reperfusion injury, spinal ischemia, central nervous system trauma, crushed or compressed optic nerve, headache, migraine, pain, multiple sclerosis, optic neuritis, optic neuropathies, ocular glaucomatous damage, epilepsy, convulsions, neurodegenerative diseases, Parkinson's disease, Alzheimer's disease, ataxias, dystonias, movement disorders, choreas, intracranial tumors, intracranial metastasis, intracranial infections, meningitis, central nervous system states in need of cognition enhancement, memory disorders, **depression**, avoidant personality disorder, **anxiety**, **panic** disorder, obsessive-compulsive disorders, phobias, impulsive disorders, cognitive disorders, mood disorders, psychoses, schizophrenia, drug abuse, chemical dependencies, drugs tolerance or withdrawal, posttraumatic stress syndrome, eating disorders, obesity premature ejaculation, hypertension, aminoglycoside antibiotics-induced hearing loss, central nervous system drug-induced disorders and states, N-methyl-D-aspartate-induced neurodegeneration, glutamate induced excitotoxic effects on nerve cells, central nervous system metabolic disorders and states, central nervous system deficiency disorders, central nervous system disorders and states amenable to neuropeptides **therapy**, central nervous system disorders and states amenable to **neurotrophic factors therapy**, central nervous system disorders and states amenable to neuroprotective **therapy**, central nervous system mediated ocular glaucomatous damage, autoimmune glaucoma, central nervous system disorders and states amenable to gene-therapy, surgically-induced inflammation, trauma-induced inflammation, angiogenesis-related disorder, hypoproliferative diseases, brain or spinal cord disease, disorder or injury, conditions which can lead to excessive glutamate release, conditions which can lead to neurodegeneration, stroke, impaired blood flow in neuronal tissue, septic or traumatic shock, hemorrhage shock, arthritis, arteriosclerosis, conditions which can lead to bursting of the myelin sheath around nerves, senile dementia, Huntington's disease, Lou Gehrig's disease (ALS), addictive disorders to at least one of alcohol, nicotine, and other psychoactive substance, adjustment disorder, age-associated learning and mental disorder, anorexia nervosa, apathy, **attention-deficit** disorder due to general medical conditions, **attention-deficit** hyperactivity disorder, **bipolar** disorder, bulimia nervosa, chronic fatigue syndrome, chronic or acute stress, conduct disorder, cyclothymic disorder, dizziness, dysthymic disorder, fibromyalgia and other somatoform disorders, incontinence, inhalation disorder, insomnia, intoxication disorder, obesity, peripheral neuropathy, **premenstrual** dysphoric disorder, psychotic disorder, seasonal affective disorder, sexual dysfunction, sleep disorder (e.g. narcolepsy and enuresis), specific developmental disorder, TIC disorders (e.g. Tourette's disease and withdrawal syndrome) (claimed).

ADVANTAGE - The method achieves effective CNS target site concentrations of the drugs, while limiting systemic exposure and distribution of the drug to peripheral sites of action. Thus lessens unwanted side effects and the potential for toxicity.

Dwg.0/8

L169 ANSWER 22 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-732904 [79] WPIDS
CROSS REFERENCE: 1999-371083 [31]; 2001-159150 [16]
DOC. NO. CPI: C2002-207476
TITLE: New adrenergic compounds useful in the treatment of, e.g. glaucoma, Crohn's disease, gastritis, diabetic neuropathy, diarrhea, hypertension or autoimmune disease.
DERWENT CLASS: B03
INVENTOR(S): BURKE, J A; CHOW, K; GARST, M E; GIL, D W; HARCOURT, D A; WHEELER, L A; GOMEZ, D G; MUNK, S A
PATENT ASSIGNEE(S): (ALLR) ALLERGAN SALES INC; (ALLR) ALLERGAN INC
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002076950	A2	20021003	(200279)*	EN	141
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003023098	A1	20030130	(200311)		
EP 1370533	A2	20031217	(200402)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CZ 2003002471	A3	20040218	(200430)		
AU 2002254265	A1	20021008	(200432)		
HU 2003003634	A2	20040428	(200435)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002076950	A2		WO 2002-US8222	20020313
US 2003023098	A1	CIP of	US 1997-985347	19971204
		CIP of	US 1998-205597	19981204
		CIP of	US 1999-329752	19990610
			US 2001-815362	20010321
EP 1370533	A2		EP 2002-723489	20020313
			WO 2002-US8222	20020313
CZ 2003002471	A3		WO 2002-US8222	20020313
			CZ 2003-2471	20020313
AU 2002254265	A1		AU 2002-254265	20020313
HU 2003003634	A2		WO 2002-US8222	20020313
			HU 2003-3634	20020313

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1370533	A2	Based on	WO 2002076950
CZ 2003002471	A3	Based on	WO 2002076950
AU 2002254265	A1	Based on	WO 2002076950
HU 2003003634	A2	Based on	WO 2002076950

PRIORITY APPLN. INFO: US 2001-815362 20010321; US 1997-985347 19971204; US 1998-205597 19981204; US

1999-329752 19990610

ED 20021209

AB WO 200276950 A UPAB: 20040603

NOVELTY - Adrenergic compounds or their salts, esters, stereoisomers or racemic mixtures are new.

DETAILED DESCRIPTION - Adrenergic compounds (A) of formula (I) or (II) or their salts, esters, stereoisomers or racemic mixtures are new.

x = 1 or 2;

R1 - R3 = Q or (CH2)n-X-(CH2)m-(R5)o;

Q = H, halo, 1-4C alkyl, 1-4C alkenyl, 1-4C alkynyl, COR4, 3-6C cycloalkyl, (hetero)aryl, cyano, nitro, trihalomethyl or oxo;

X and Y1 = O, S or N;

R4 = H, 1-4C alkyl or 1-4C alkoxy;

m and n = 0 - 3;

o = 0 or 1;

R5 = methyl or H1-2;

R2+R3 = optionally saturated ring of formula (C(R6)p)q-Xs-(C(R6)p)r-Xt-(C(R6)p)u;

R6 = Q;

p = 1 - 2;

q, r and u = 0 - 5;

s = 0 - 1;

Y = X or -(C(R7)z)s';

z = 1 - 2;

s' = 1 - 3;

R7 = R1, CH=, CH=CH- or Y1CH2;

a = single or double bond;

q+r+u+s+t = less than 6.

Provided that:

(i) when the ring containing Y is cyclohexane or heterocyclic 5 membered ring, then the ring is not fully unsaturated; and

(ii) when Y is O, N or S, then the ring containing Y contains at least one double bond.

ACTIVITY - Antiinflammatory; Analgesic; Cytostatic; Antidiabetic; Neuroprotective; Antidiarrheic; Vasotropic; Cerebroprotective; Nootropic; Tranquilizer; Antidepressant; Hypotensive; Cardiant; Antiarthritic; Antirheumatic; Osteopathic; Antigout; Immunosuppressive; Dermatological; Ophthalmological.

No biological data available.

MECHANISM OF ACTION - alpha -2B and alpha -2B/2C adrenergic receptor subtype agonist. 4-(3-Ethyl-cyclohex-2-enylmethyl)-1H-imidazole (A) was tested for approx. 2B/2C adrenergic receptor agonistic activity using Receptor Selection and Amplification Technology (RSAT) assay as described in Massier et al. (1995) High throughput assays of cloned adrenergic, muscarinic, neurokinin and **neurotrophin** receptors in living mammalian cells, **Pharmacol**. Toxicol. 76:308 - 11. NIH-3T3 cells were plated and maintained in Dulbecco's modified Eagle's medium supplemented with 10% calf serum. One day later, the cells were cotransfected by calcium phosphate precipitation with mammalian expression plasmid encoding p-SV- beta -galactosidase, receptor and G-protein. Salmon sperm DNA (40 mg) were included and the cells were harvested, frozen. The cells were thawed and added to various concentrations of (A) and incubated for 72 - 96 hours at 37 deg. C.

(A) showed an EC50 of 0.7 and 0.3 at alpha 2B and approx. 2C adrenergic receptor subtype respectively.

USE - (A) are used in the treatment of glaucoma, sedation, cardiovascular **depression**, chronic gastrointestinal inflammation, Crohn's disease, gastritis, irritable bowel disease, ulcerative colitis, visceral pain including pain caused by cancer, neuropathic pain, neuralgia, herpes, deafferentation pain, diabetic neuropathy, diarrhea, nasal congestion, hyperactive micturition, diuresis, withdrawal syndrome, neurodegenerative disease including optic neuropathy,

spinal ischemia, stroke, memory and cognition deficits, **attention deficit** disorder, psychoses including **manic** disorders, **anxiety**, **depression**, hypertension, congestive heart failure, cardiac ischemia, arthritis including rheumatoid arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune disease such as lupus erythematosus, hyperemia, conjunctivitis or uveitis.

ADVANTAGE - (A) exhibit selective agonistic activity at alpha 2B and alpha 2B/2C adrenergic receptor subtype(s) over the alpha 2A adrenergic receptor subtype. (A) have substantial analgesic activity regardless of the origin with minimum side effects and reduce elevated intraocular pressure.

Dwg.0/0

L169 ANSWER 23 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-454828 [48] WPIDS
DOC. NO. CPI: C2002-129387
TITLE: Use of amphetamine compound for enhancing long-term memory and for treatment of e.g. **anxiety**, **depression**, age-associated memory impairment, amnesia, dementia, learning difficulties and Parkinson's disease.
DERWENT CLASS: B05
INVENTOR(S): EPSTEIN, M; WIIG, K A; EPSTEIN, M H
PATENT ASSIGNEE(S): (SENT-N) SENTION INC; (EPST-I) EPSTEIN M; (WIIG-I) WIIG K A; (EPST-I) EPSTEIN M H
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002039998	A2	20020523	(200248)*	EN	130
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
US 2002115725	A1	20020822	(200258)		
AU 2002039464	A	20020527	(200261)		
US 2003119884	A1	20030626	(200343)		
US 2003232890	A1	20031218	(200401)		
EP 1420768	A2	20040526	(200435)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002039998	A2		WO 2001-US45793	20011031
US 2002115725	A1	Provisional	US 2000-245323P	20001101
			US 2001-3740	20011031
AU 2002039464	A		AU 2002-39464	20011031
US 2003119884	A1	Provisional	US 2000-245323P	20001101
		CIP of	US 2001-3740	20011031
			US 2002-139606	20020502
US 2003232890	A1	Provisional	US 2000-245323P	20001101
		CIP of	US 2001-3740	20011031
		CIP of	US 2002-139606	20020502
			US 2003-444970	20030523
EP 1420768	A2		EP 2001-987226	20011031

WO 2001-US45793 20011031

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002039464	A Based on	WO 2002039998
EP 1420768	A2 Based on	WO 2002039998

PRIORITY APPLN. INFO: US 2000-245323P 20001101; US 2001-3740 20011031

ED 20020730

AB WO 200239998 A UPAB: 20020730

NOVELTY - Pharmaceutical preparation comprises at least one amphetamine compound.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) A kit comprising the preparation; and

(2) Conducting a pharmaceutical business involving either:

(i) manufacturing the kit; and

(ii) marketing to healthcare providers the benefits of using the kit or preparation to enhance memory of treated patients;

(iii) providing a distribution network for selling the kit; and

(iv) providing instruction material to patients or physicians for using it or preparation to enhance memory of treated patients;

(v) determining an appropriate dosage of the amphetamine compound to enhance memory function in a class of patients;

(vi) conducting therapeutic profiling of at least one formulation of step (v) for efficacy and toxicity in animals; and

(vii) providing a distribution network for selling the formulation of step (vi); or

(viii) the step (v); and

(ix) licensing to a third party the rights for further development and sale of the amphetamine compound for enhancing memory.

ACTIVITY - Tranqulizer; Antidepressant; Nootropic; Antiparkinsonian; Vulnerary; Anticonvulsant; Cerebroprotective; Neuroleptic; Neuroprotective; Anti-HIV.

MECHANISM OF ACTION - None given.

USE - In the manufacture of a medicament for treatment of an animal (preferably mammal, particularly human) susceptible to or suffering from **anxiety**, **depression**, age-associated memory impairment, minimal cognitive impairment, amnesia, dementia, learning disabilities, memory impairment associated with toxicant exposure, brain injury, brain aneurysm, Parkinson's disease, head trauma, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, stroke, schizophrenia, epilepsy, mental retardation, Alzheimer's disease, age, **attention deficit** disorder, **attention deficit** hyperactivity disorder, or AIDS-related dementia (all claimed).

ADVANTAGE - The preparation is formulated for sustained release of the amphetamine to enhance long-term memory in a patient but resulting in a concentration in the patient lower than its EC50 as a CNS stimulant. The preparation enhances long-term memory in a patient by statistically significant amount when assessed by a at least one of standardized performance test; Cambridge Neuropsychological Test Automated Battery (CANTAB); a Children's Memory Scale (CMS); a Contextual Memory Test; a Continuous Recognition Memory Test (CMRT); a Denman Neuropsychology Memory Scale; a Fuld Object; Memory Evaluation (FOME); a Graham-Kendall Memory for Designs Test; a Guild Memory Test; a Learning and Memory Battery (LAMB); a Memory Assessment Clinic Self Rating Scale (MAC-S); a Memory Assessment Scales (MAS); a Randt Memory Test; a Recognition Memory Test (RMT); a Rivermead Behavioral Memory Test; a Russell's Version of the Wechsler Memory Scale (RWMS); a Test of Memory and Learning (TOMAL); a

Vermont Memory Scale (VMS); a Wechsler Memory Scale; and a Wide Range Assessment of Memory and Learning (WRAML).
Dwg.0/16

L169 ANSWER 24 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-291790 [33] WPIDS
DOC. NO. CPI: C2002-085632
TITLE: Isolated **neurotrophic factor** useful for **treating** neurological conditions is present in a medium containing Schwann cells culture.
DERWENT CLASS: A96 B04
INVENTOR(S): BENOWITZ, L I; IRWIN, C A; JACKSON, P
PATENT ASSIGNEE(S): (CHIL-N) CHILDRENS MEDICAL CENT
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002006341	A1	20020124	(200233)*	EN	50

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001080566 A 20020130 (200236)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002006341	A1	WO 2001-US22315	20010716
AU 2001080566	A	AU 2001-80566	20010716

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001080566	A	Based on	WO 2002006341

PRIORITY APPLN. INFO: US 2000-616287 20000714
ED 20020524
AB WO 200206341 A UPAB: 20020524
NOVELTY - An isolated neurotrophic factor (I) of the type that is present in a medium containing Schwann cells culture is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a method for producing a neurosalutary effect in a subject by **administering** the **neurotrophic factor** (I) to the subject; and

(2) a method for treating neurological disorder involving administering (I) to a subject suffering from the neurological disorder.

ACTIVITY - Anticonvulsant; Nootropic; Neuroprotective; Cerebroprotective; Tranquilizer; Vulnerary; Neuroleptic; Antidepressant; Antidiabetic; Antiparkinsonian; Antimanic; Hypotensive; Analgesic; Antibacterial; Antiinflammatory; Antipyretic; Anti-HIV.

MECHANISM OF ACTION - Axonal outgrowth of naive goldfish retinal ganglion cells stimulator; Axonal outgrowth of embryonic rat spinal cord neuron stimulator; Modulators of neuronal survival, neuronal regeneration and neuronal axonal outgrowth of central nervous system neurons such as retinal ganglion cells.

USE - For producing neurosalutory effect in a subject such as mammal

e.g. human suffering from a neurological disorder such as spinal cord injury, e.g. monoplegia, diplegia, paraplegia, hemiplegia, or quadriplegia, epilepsy e.g. posttraumatic epilepsy, Alzheimer's disease (all claimed). The neurological disorders include traumatic or toxic injuries to peripheral or cranial nerves, traumatic brain injury, stroke, cerebral aneurism, cognitive and neurodegenerative disorders such as dementias, Huntington's disease, Gilles de la Tourette's syndrome, multiple sclerosis, amyotrophic, lateral sclerosis, hereditary motor and sensory neuropathy (Charcot-Marie-Tooth disease), diabetic neuropathy, progressive supranuclear palsy, Jakob-Creutzfeldt disease or disorders included in Harrison's Principles of Internal Medicine (Braunwald et-al.McGraw-Hill,2001) and in the American Psychiatric Association's Diagmestic and statistical manual of mental Disorders DSM-IV (American Psychiatric Press,2000); for treating hypertension and sleep disorders, neuropsychiatric disorders such as **depression**, schizophrenia, schizoaffective disorder, korsakoff's psychosis, mania, **anxiety** disorders, or phobic disorder, learning or memory disorders (such as amnesia and age-related memory loss), **attention deficit** disorder, dysthymic disorder, major **depressive disorder** , **mania**, obsessive compulsive disorder, psychoactive substance, use disorder, **panic** disorder, **bipolar** affective disorder, psychogenic pain syndromes, and eating disorders; for treating injuries of nervous system due to an infections disease (such as meningitis, high fever of various etiologies, HIV, syphilis, or post-polio syndrome) or due to electricity (including contact with electricity or lightening and complications from electro-convulsive psychiatric therapy); for preventing or treating neurological deficits in embryos or fetuses in utero, in premature infants, or in children with need of such treatment, including those with neurological birth defects.

ADVANTAGE - The formulation provides sustained delivery of (I) for at least one-week (preferably at least one month) after the formulation is **administered** to the subject. The **neurotrophic factor** stimulates axonal outgrowth of naive goldfish retinal ganglion cells, embryonic rat spinal cord neurons and passes through a centrifugal filter with a 1 kDa cut-off. The neurotrophic factor further fails to bind to a 18C reversed-phase HPLC column, forms a compound that elutes from a reverse-phase HPLC column, at 23 minutes, after being chemically derivatized with AQC and has an elution time of 6 minutes on a G10-Sepharose size-exclusive column.

Dwg.0/5

L169 ANSWER 25 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-300327 [31] WPIDS
DOC. NO. CPI: C2001-092239
TITLE: Novel polynucleotides that modulate **nerve growth factor** metabolism useful for **treating** Alzheimer's disease, diabetic neuropathy, congenital insensitivity to pain, and hyperalgesia associated with NGF therapy.
DERWENT CLASS: B04 D16
INVENTOR(S): HALEGOUA, S; HASEL, K W; HILBUSH, B
PATENT ASSIGNEE(S): (DIGI-N) DIGITAL GENE TECHNOLOGIES INC
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001029179	A2	20010426	(200131)*	EN	123

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001012226 A 20010430 (200148)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001029179	A2	WO 2000-US29131	20001020
AU 2001012226	A	AU 2001-12226	20001020

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001012226	A	Based on	WO 2001029179

PRIORITY APPLN. INFO: US 1999-160562P 19991020
ED 20010607
AB WO 200129179 A UPAB: 20010607
NOVELTY - An isolated nucleic acid (I) molecule that effectively modulates nerve growth factor (NGF), comprising a polynucleotide sequence (S1) selected from any one of the 30 sequences of length ranging from 75-3437 nucleotides fully defined in the specification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polypeptide (II) encoded by (I);
(2) an isolated nucleic acid molecule (Ia) comprising a polynucleotide at least 95% identical to (I), a sequence of at least ten bases in length that is hybridizable to (I) under stringent conditions, a sequence encoding (II) or its fragment, a sequence encoding a polypeptide epitope of (II), or a sequence encoding a species homolog of (II);
(3) a recombinant vector (III) comprising (I);
(4) a recombinant host cell (IV) comprising (I);
(5) making (IV);
(6) an isolated antibody (Ab) that binds specifically to (II);
(7) a recombinant host cell (IVa) that expresses (II);
(8) an isolated polypeptide produced by culturing (IV) under conditions such that (II) is expressed and isolating the polypeptide;
(9) diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, by determining the presence or absence of a mutation in (II), or by detecting an alteration in expression of a polypeptide encoded by (II);
(10) identifying a binding partner to (II), by contacting (II) with a binding partner, and determining whether the binding partner affects the activity of the polypeptide;
(11) a gene corresponding to the cDNA sequence of (I);
(12) identifying activity of an expressed polypeptide in a biological assay, by expressing (II) in a cell, isolating the expressed polypeptide, testing the expressed polypeptide for an activity in a biological assay, and identifying the activity of the expressed polypeptide based on the test results;
(13) a substantially pure isolated DNA molecule suitable for use as a probe for genes regulated in a disorder of neuronal differentiation, chosen from the DNA molecules that are fully defined in the specification, having a 5' partial nucleotide sequence and length as described by their digital address, and having a characteristic regulation pattern in response of PC12 cells to NGF;
(14) a kit (K) for detecting the presence of (II) in a mammalian tissue sample comprising a first antibody which immunoreacts with a mammalian protein encoded by a gene corresponding to (II) or with a polypeptide encoded by (II) in an amount sufficient for at least one assay

and suitable packaging material;

(15) a kit for detecting the presence of a gene encoding a protein comprising (II) or its fragment having at least 10 contiguous bases, in an amount sufficient for at least one assay, and suitable packaging material; and

(16) detecting the presence of a nucleic acid encoding a protein in a mammalian tissue sample, by hybridizing (II) or its fragment having at least 10 contiguous bases, with the nucleic acid of the sample and detecting the presence of the hybridization product.

ACTIVITY - Nootropic; neuroprotective; neuroleptic; tranquilizer; antidiabetic; vulnerary; antiHIV; antianemic; cytostatic; anticoagulant; thrombostatic; hemostatic; nephrotropic; antirheumatic; antiarthritic; dermatological; antiallergic; antiinflammatory; antiaddictive; antialcoholic; antidepressant; antiasthmatic; immunosuppressive.

MECHANISM OF ACTION - Neuromodulator; gene therapy. No supporting data given.

USE - (I), (II) and Ab are useful for preventing, treating, modulating, or ameliorating a disorder of altered target cell metabolism of NGF, Alzheimer's disease, diabetic neuropathy, congenital insensitivity to pain with anhidrosis, side effect of NGF therapy, and hyperalgesia associated with NGF therapy. (I), (II) and Ab are also useful in the manufacture of a medicament for the treatment of a disorder of altered target cell metabolism of NGF (claimed). (I) is useful as chromosomal marker for chromosome identification, in gene therapy, for identifying individuals from minute biological samples, as molecular weight markers on southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to discover novel polynucleotides, for selecting and making oligomers for attachment to a gene chip or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as antigens to elicit immune response. (II) is useful for generating fusion proteins, to assay protein levels in a biological sample, as antigens to trigger immune response and for treating diseases. (I) and (II) are useful for treating and preventing deficiencies or disorders of the central nervous system or peripheral nervous system, for diagnosing disorders such as Alzheimer's disease, Pick's disease, Binswanger's disease, other senile dementia, Parkinson's disease, Parkinsonism, obsessive compulsive disorders, epilepsy, encephalopathy, ischemia, alcohol addiction, drug addiction, schizophrenia, amyotrophic lateral sclerosis, multiple sclerosis, **depression** and **bipolar manic-depressive disorder**, to study circadian variation, aging or long-term potentiation, the latter affecting the hippocampus, to study brain regions that are known to be involved in complex behaviors, such as learning and memory, emotion, drug addition, glutamate neurotoxicity, feeding behavior, olfaction, viral infection, vision, and movement disorders. (I) or (II) is useful in treating deficiencies or disorders of the immune system, hematopoietic cells, to modulate hemostatic or thrombolytic activity, treatment or detection of autoimmune disorders e.g., Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, allergic reaction and conditions, such as asthma, organ rejection or graft-versus host disease (GVHD), to modulate inflammation, to treat inflammatory conditions, and both chronic and acute conditions. (I) or (II) can be useful to treat or detect hyperproliferative disorders, including neoplasms and to treat or detect infectious agents. (I) or (II) is useful to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (I) and (II) are also useful for increase or decrease the differentiation or proliferation of embryonic stem cells from a lineage other than the above-described hemopoietic lineage, to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size and shape, to modulate mammalian metabolism affecting catabolism, anabolism processing,

utilization, and storage of energy, to change a mammal's mental state or physical state, and as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors, or other nutritional components.
Dwg.0/14

L169 ANSWER 26 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-399923 [34] WPIDS
DOC. NO. CPI: C2000-120752
TITLE: Composition useful for enhancing neurite outgrowth, neuronal survival and neuronal proliferation comprises a triazole compound and a neurotrophic factor.
DERWENT CLASS: B03 B04
INVENTOR(S): GAGE, F H; GUILLEMIN, R C; RAY, J; GUILLEMIN, R C L
PATENT ASSIGNEE(S): (SALK) SALK INST BIOLOGICAL STUDIES
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000030656	A1	20000602	(200034)*	EN	53
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000020269	A	20000613	(200043)		
US 6680292	B1	20040120	(200407)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000030656	A1	WO 1999-US27475	19991119
AU 2000020269	A	AU 2000-20269	19991119
US 6680292	B1 Provisional	US 1998-109308P	19981120
		US 2001-856100	20010924

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000020269	A Based on	WO 2000030656

PRIORITY APPLN. INFO: US 1998-109308P 19981120; US 2001-856100 20010924
ED 20000718
AB WO 200030656 A UPAB: 20000718
NOVELTY - Composition comprising a 1- (beta-D-ribofuranosyl)-1H-1,2,4-triazole and a neurotrophic factor, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method of enhancing endogenous **neurotrophic factor** activity comprising **administration** of 1-(beta-D-ribofuranosyl)-1H-1,2,4-triazole.
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; CNS-Gen.; Antimicrobial-Gen.; Antiinflammatory; Cytostatic; Cerebroprotective; Muscular-Gen.; Antidepressant; Neuroleptic; Antimanic; Anorectic; Respiratory-Gen.; Analgesic; Eating-Disorders-Gen.; Endocrine-Gen.; Antiaddictive; Tranquilizer; Dermatological; Ophthalmological; Vasotropic; Immunosuppressive; Antiasthmatic;

Antiarrhythmic.

The ability of (I) to stimulate neurite elongation as determined by growth cone turning was evaluated in vitro. Cells growing in culture were exposed to a focal site of ribavirin and control compounds and the number of growth cones with a turning angle was measured and the turned angle of each growth cone was measured. Ribavirin stimulated growth cone turning compared to control substances.

USE - The composition is useful for enhancing neurite outgrowth, neuronal survival and neuronal proliferation; treating neurological diseases such as Alzheimer's disease, Parkinson's disease, multiple sclerosis and Huntington's disease; and treating neuronal trauma (claimed). It is also useful for treating acute, subacute or chronic injury to the nervous system, acute brain injury (eg. stroke and cerebral palsy), and a large number of CNS dysfunctions (eg. **depression**, epilepsy and schizophrenia). Further diseases contemplated for treatment include psychiatric disorders, obesity, disorders of respiration, motor control and function, pain disorders, eating disorders, sexual disorders, drug withdrawal, drug addiction, **anxiety**, skin disorders, retinal ischemia, glaucoma, disorders associated with organ transplantation, asthma and astrocytomas.

ADVANTAGE - It is advantageous to enhance the ability of growth factors to stimulate neuronal replication, increase neuronal survival and stimulate growth of neuronal processes by an agent that is amenable to pharmacological manipulation. Furthermore, a non-naturally occurring molecule is advantageous in order to increase selectivity for neuronal cells and decrease the potential for adverse side effects.

Dwg.0/8

L169 ANSWER 27 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-060014 [05] WPIDS
DOC. NO. CPI: C1999-017805
TITLE: Nanoparticle targeting system for therapeutic and diagnostic drugs - notably across blood or brain barrier for CNS disorders, diagnosis and radiation therapy, uses stabiliser for particles.
DERWENT CLASS: A96 B07
INVENTOR(S): SABEL, B A; SCHROEDER, U
PATENT ASSIGNEE(S): (MEDI-N) MEDINOVA MEDICAL CONSULTING GMBH; (SABE-I) SABEL B A; (SCHR-I) SCHROEDER U; (NANO-N) NANOPHARM AG
COUNTRY COUNT: 78
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9856361	A1	19981217	(199905)*	EN	43
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU					
AU 9731760	A	19981230	(199920)		
EP 986373	A1	20000322	(200019)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2001502721	W	20010227	(200115)		42
KR 2001013745	A	20010226	(200154)		
US 2002034474	A1	20020321	(200224)		
US 2003152636	A1	20030814	(200355)		
EP 986373	B1	20040317	(200421)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69728179	E	20040422	(200428)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9856361	A1	WO 1997-EP3099	19970613
AU 9731760	A	AU 1997-31760	19970613
		WO 1997-EP3099	19970613
EP 986373	A1	EP 1997-927181	19970613
		WO 1997-EP3099	19970613
JP 2001502721	W	WO 1997-EP3099	19970613
		JP 1999-501359	19970613
KR 2001013745	A	WO 1997-EP3099	19970613
		KR 1999-711760	19991213
US 2002034474	A1	WO 1997-EP3099	19970613
		US 2000-445439	20000223
US 2003152636	A1 Div ex	WO 1997-EP3099	19970613
	Div ex	US 2000-445439	20000223
		US 2003-383559	20030310
EP 986373	B1	EP 1997-927181	19970613
		WO 1997-EP3099	19970613
DE 69728179	E	DE 1997-628179	19970613
		EP 1997-927181	19970613
		WO 1997-EP3099	19970613

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9731760	A Based on	WO 9856361
EP 986373	A1 Based on	WO 9856361
JP 2001502721	W Based on	WO 9856361
EP 986373	B1 Based on	WO 9856361
DE 69728179	E Based on	EP 986373
	Based on	WO 9856361

PRIORITY APPLN. INFO: WO 1997-EP3099 19970613
ED 19990203
AB WO 9856361 A UPAB: 19990203
Drug targeting delivery system for administration to a mammal, comprises nanoparticles containing: (a) polymeric material; (b) one or more physiologically active substances; and (c) one or more stabilisers, allowing transport of the bioactive substance to a specific site within or on the body; also a carrier and/or diluent as transport medium, is new.

USE - A wide variety of drugs can be administered to humans and other mammals by various routes using the system, including oral, or by injection, suppository, or inhalation, usually by oral or intravenous injection or infusion. Notably, the system allows non-penetrating or poorly penetrating drugs with potent activities to cross the blood/brain barrier without the need for chemical modification or specific carriers to permit transit. Examples of these drugs, for treatment of CNS disorders, include those acting at synaptic and neuroeffector junction sites, general and local analgesics, hypnotics and sedatives, cerebral dilators, psychiatric or psychotropic drugs for treatment of **depression**, schizophrenia, **mania**, migraine, and epilepsy (anticonvulsants), those for treatment of Alzheimer's, Parkinson's, and Huntington's diseases and aging, excitatory amino acid antagonists, **neurotrophic factors** and neuroregenerative agents, trophic factors, those for **treatment** of CNS trauma or stroke, those for treatment of addiction and drug abuse, and diagnostics, notably in the nuclear medicine area, also for radiation therapy, both also of value in other parts of the body. Examples of non-CNS active drugs include antacids, antiinflammatories, antimicrobials and antiparasitics, immunomodulators, cytostats and other anticancer drugs, hormones and hormone antagonists,

heavy metals and antagonists either for them or non-metallic toxins, transmitters and their receptor agonists and antagonists, transporter inhibitors, antibiotics, antispasmodics, antihistamines, antinauseants, relaxants and stimulants, sense and antisense oligonucleotides, vascular dilators and costrictors, antihypertensives, hyperglycaemic and hypoglycaemic agents, antiasthmatics, and anti-obesity drugs. A further class includes vitamins, minerals, and nutritional agents.

ADVANTAGE - The system requires no surfactant, as in a prior art system used for this purpose. Manufacture is simplified, and the possibility of toxic effects from the surfactant, or of direct injection of a drug into the brain, eliminated.

Dwg.4/5

L169 ANSWER 28 OF 39 EMBASE
on STN

ACCESSION NUMBER: 2003336671 EMBASE
TITLE: Opinion and evidence in neurology and psychiatry.
SOURCE: CNS Drugs, (2003) 17/10 (763-769).
Refs: 3
ISSN: 1172-7047 CODEN: CNDREF
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The management of neurological and psychiatric disorders is a vast and evolving area for researchers, primary care physicians and specialists. To help you keep up to date with the latest advances worldwide on all aspects of drug therapy for neurological and psychiatric disorders, this section of the journal brings you information selected from the drug therapy reporting service Inpharma Weekly. The following reports are selected from the latest issues, summarising the most important research and development news, clinical studies, treatment guidelines, pharmacological, pharmacoeconomic and adverse drug reactions/interactions news, and expert opinion pieces published across a broad range of literature sources.

L169 ANSWER 29 OF 39 EMBASE
on STN

ACCESSION NUMBER: 2003363877 EMBASE
TITLE: Psychiatric Drug Discovery & Development - SRI Conference: 23-24 June, 2003, Princeton, NJ, USA.
AUTHOR: Vanover K.E.
CORPORATE SOURCE: K.E. Vanover, ACADIA Pharmaceuticals Inc., 3911 Sorrento Valley Boulevard, San Diego, CA 92121, United States. kvanover@acadia-pharm.com
SOURCE: IDrugs, (1 Aug 2003) 6/8 (739-742).
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 032 Psychiatry
022 Human Genetics
030 Pharmacology
038 Adverse Reactions Titles
014 Radiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Overall, this meeting was interesting and informative. Neurogenesis as a

predictive model for antidepressant efficacy appears to be growing as part of early drug discovery efforts in combination with behavioral assays for selecting compounds to take forward into the clinic. In addition, there was considerable discussion on differentiation between the subtypes of different disorders, for example, separating schizophrenics into 'deficit' and 'non-deficit' subtypes or distinguishing generalized anxiety disorders from stress-related anxiety disorders and depression. The current focus is on genetic and animal models to facilitate the discovery of new drugs for treating specific subpopulations of patients.

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ACCESSION NUMBER: 2002420945 EMBASE
TITLE: Alzheimer's disease and the basal forebrain cholinergic system: Relations to .beta.-amyloid peptides, cognition, and treatment strategies.
AUTHOR: Auld D.S.; Kornecook T.J.; Bastianetto S.; Quirion R.
CORPORATE SOURCE: R. Quirion, Douglas Hospital Research Centre, 6875 Blvd. Lasalle, Verdun, Que. H4H IR3, Canada. quirem@douglas.mcgill.ca
SOURCE: Progress in Neurobiology, (2002) 68/3 (209-245). Refs: 504
ISSN: 0301-0082 CODEN: PGNBA5
PUBLISHER IDENT.: S 0301-0082(02)00079-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Alzheimer's disease (AD) is the most common form of degenerative dementia and is characterized by progressive impairment in cognitive function during mid- to late-adult life. Brains from AD patients show several distinct neuropathological features, including extracellular .beta.-amyloid-containing plaques, intracellular neurofibrillary tangles composed of abnormally phosphorylated .tau., and degeneration of cholinergic neurons of the basal forebrain. In this review, we will present evidence implicating involvement of the basal forebrain cholinergic system in AD pathogenesis and its accompanying cognitive deficits. We will initially discuss recent results indicating a link between cholinergic mechanisms and the pathogenic events that characterize AD, notably amyloid-.beta. peptides. Following this, animal models of dementia will be discussed in light of the relationship between basal forebrain cholinergic hypofunction and cognitive impairments in AD. Finally, past, present, and future treatment strategies aimed at alleviating the cognitive symptomatology of AD by improving basal forebrain cholinergic function will be addressed. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.

L169 ANSWER 31 OF 39 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001191793 EMBASE
TITLE: Amyotrophic lateral sclerosis.
AUTHOR: Rowland L.P.; Shneider N.A.
CORPORATE SOURCE: Dr. L.P. Rowland, Neurological Institute, Columbia-Presbyterian Medical Center, 701 W. 168th St., New York, NY 10032, United States. lprl@columbia.edu
SOURCE: New England Journal of Medicine, (31 May 2001) 344/22 (1688-1700).

Refs: 148
ISSN: 0028-4793 CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English

L169 ANSWER 32 OF 39 EMBASE
on STN

ACCESSION NUMBER: 2001287363 EMBASE
TITLE: Does vascular disease cause late-life depression?.
AUTHOR: Alexopoulos G.S.
CORPORATE SOURCE: Dr. G.S. Alexopoulos, Weill Medical College, Cornell University in New York, Cornell Inst. of Geriatric Psychiat., White Plains, NY, United States
SOURCE: Economics of Neuroscience, (2001) 3/7 (49-56).
Refs: 113
ISSN: 1527-0815 CODEN: ENCEBO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A confluence of findings suggests that cerebrovascular disease may predispose, precipitate, or perpetuate some late-life depressive syndromes. Compromised integrity of frontostriatal neural systems and their limbic and hippocampal connections appears to be a central abnormality. This view is supported by the presentation of "vascular depression," which consists of depressive symptoms, cognitive abnormalities, and structural and functional neuroimaging findings. Vascular depression may be caused by critical lesions or an accumulation of lesions leading to disruption of frontostriatal pathways or their modulating systems. Emerging evidence suggests that the "depression-executive dysfunction syndrome," a condition often caused by vascular depression, has a poor or slow response to antidepressant treatment and a high risk for relapse and recurrence. The vascular depression hypothesis, while it cannot be directly tested, provides the rationale for treatment and prevention studies of late-life depression. The efficacy of agents acting on neurotransmitter systems related to frontostriatal dysfunction such as dopamine, acetylcholine, and opioid neurotransmission can be studied in vascular depression. Drugs used for prevention and treatment of cerebrovascular disease could be shown to reduce the risk for vascular depression or improve its long-term outcomes. Conventional antidepressants have different effects on the neurologic recovery process following cerebrovascular lesions. Appropriate research may guide the selection of antidepressants in patients with vascular depression who are candidates for new ischemic events. Awareness of interactions among specific symptoms, cognitive deficits, and disability may lead to interventions that target a patient's deficits and even psychosocial factors known to contribute to depression. Study of the hemodynamic disturbances underlying vascular depression may result in a pathophysiologically based definition of vascular depression that can be used for clinical diagnosis and focused treatment.

L169 ANSWER 33 OF 39 EMBASE
on STN
ACCESSION NUMBER: 1998097042 EMBASE
TITLE: Comprehensive management of amyotrophic lateral sclerosis.
AUTHOR: Carter G.T.; Miller R.G.
CORPORATE SOURCE: Dr. G.T. Carter, 500 SE Washington, Chehalis, WA 98532, United States
SOURCE: Physical Medicine and Rehabilitation Clinics of North America, (1998) 9/1 (271-284).
Refs: 48
ISSN: 1047-9651 CODEN: PMRAFZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Amyotrophic lateral sclerosis (ALS) is a rapidly progressive motor neuron disease that poses a myriad of clinical problems. Patients with ALS are best treated in a multidisciplinary setting involving physicians, clinical nursing specialists, and physical, occupational, speech, and respiratory therapists, as well as psychologists and social workers. Palliative and rehabilitative strategies may ease suffering, while new treatments provide hope for effective treatment of this disease.

L169 ANSWER 34 OF 39 EMBASE
on STN
ACCESSION NUMBER: 96216671 EMBASE
DOCUMENT NUMBER: 1996216671
TITLE: Is there a role for estrogen replacement therapy in the prevention and treatment of dementia?.
AUTHOR: Birge S.J.; Kuller L.H.
CORPORATE SOURCE: Div. of Geriatrics and Gerontology, Washington Univ. School of Medicine, 216 S. Kingshighway Blvd.,St. Louis, MO 63110, United States
SOURCE: Journal of the American Geriatrics Society, (1996) 44/7 (865-870+878-880).
ISSN: 0002-8614 CODEN: JAGSAF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Studies in experimental animal models provide a convincing rationale for a role for ERT in the treatment and prevention of dementia. These studies establish the role of estrogen in the regeneration and preservation of neuronal elements within the CNS that are analogous to those regions of the brain most sensitive to the neurodegenerative changes associated with AD. Furthermore, behavioral studies in these animals establish a correlation between the hormone dependent changes in the neuronal architecture and learning and memory. However, extrapolation of these studies to postmenopausal women must be done with caution. Surgical and natural loss of ovarian function does not result in a clinically relevant decline in cognitive function over the short term (1 to 2 decades) or ever in some women. The modest changes that are observed may relate to the hormone's effect on neurotransmitter levels or their receptors. Although Singh et al. noted changes in neurotransmitter concentrations 5 weeks

after ovariectomy, changes in cognitive performance in their rat model did not become significant until 28 week after ovariectomy-the equivalent of approximately 2 decades of human life. Except for the familial forms of the disease, AD is rarely seen in the first 2 decades after the menopause. However, by the third decade after the menopause, 50% of women can be expected to manifest the histopathological changes of AD. Approximately half of these women are without clinical evidence of disease. Thus, the neurodegenerative process of AD probably precedes by many years the age of onset of the disease. We do not know what factors contribute to the selective neuronal injury which, over time, eventually leads to the neuronal loss and reduced synaptic density that result in the cognitive impairment of AD. At this time we can only speculate as to estrogen's role in modifying this process. Data from experimental animal models suggest that estrogen deficiency would selectively increase the vulnerability of estrogen-responsive neural elements, for example, the cholinergic neurons of the basal forebrain and hippocampus-a vulnerability mediated perhaps by the reduced expression of neurotrophic factors, decreased clearance of the amyloid protein, and/or reduced cerebral blood flow that are associated with estrogen deficiency. The brain's ability to adapt to the neuronal loss by stimulating axonal and synaptic regeneration would also be impaired by estrogen deficiency as suggested by estrogen's ability to restore the synaptic density of lesioned brains of ovariectomized animals. Thus, estrogen deficiency, like the apolipoprotein E4 allele, can be considered not a cause of AD but one of perhaps several factors modifying the neuronal injury and loss leading to AD. The limited epidemiologic data and intervention trials currently available are consistent with this interpretation. Because of the urgency and enormity of the problem of dementia in our aging society, there would now appear to be sufficient reason to allocate the resources needed to conduct the appropriate clinical trials to determine estrogen's efficacy in both the treatment and prevention of this devastating condition. These trials are needed so that women and their physicians can adequately weigh the risks and benefits of hormone replacement for the treatment and, more importantly, the prevention of dementia.

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ACCESSION NUMBER: 94157697 EMBASE
DOCUMENT NUMBER: 1994157697
TITLE: Pharmacotherapy for Alzheimer's disease.
AUTHOR: Whitehouse P.J.; Geldmacher D.S.
CORPORATE SOURCE: Alzheimer Center, 11100 Euclid Avenue,Cleveland, OH 44106, United States
SOURCE: Clinics in Geriatric Medicine, (1994) 10/2 (339-350). ISSN: 0749-0690 CODEN: CGMEE6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Pharmacotherapy that is effective for AD is a major goal of extensive research programs throughout the world. With the approval of tacrine in the United States, an agent is now available that has demonstrated improvement in cognition for some AD patients. Other similar symptomatic therapies are likely to become available in the near future. In the long term, prevention and cure will be based on understanding pathogenesis, such as the genetic defects that can lead to disease in some families.

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ACCESSION NUMBER: 94092130 EMBASE
DOCUMENT NUMBER: 1994092130
TITLE: Alzheimer's disease: Treatments on the horizon.
AUTHOR: Whitehouse P.J.
CORPORATE SOURCE: University Hospitals of Cleveland, Case Western Reserve University,Cleveland, OH, United States
SOURCE: P and T, (1994) 19/2 (153-155+159-160+164-165).
ISSN: 1052-1372 CODEN: PPTTEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Alzheimer's disease (AD) and related degenerative dementias present a major scientific and social challenge to all nations whose populations are aging rapidly. In the short term, neurotransmitter replacement strategies will likely dominate an effort to develop therapies that treat AD's symptoms. In the long term, an understanding of the pathogenesis of the disorder and the mechanisms by which amyloid processing is affected by genetic mutations will contribute to the development of interventions that may lead to prevention and cure. The cardinal feature of AD is a degeneration of nerve cells and their synapses associated with progressive cognitive impairment. Intermediate strategies will lead to such approaches as the use of growth factors to enhance the viability of nerve cells at risk in the disorder.

L169 ANSWER 37 OF 39 EMBASE
on STN
ACCESSION NUMBER: 93223838 EMBASE
DOCUMENT NUMBER: 1993223838
TITLE: Serotonin and neurodegenerative disorders.
SOURCE: Current Opinion in Therapeutic Patents, (1993) 3/6 (865-867).
ISSN: 0962-2594 CODEN: COTPES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L169 ANSWER 38 OF 39 EMBASE
on STN
ACCESSION NUMBER: 93344036 EMBASE
DOCUMENT NUMBER: 1993344036
TITLE: Central nervous system drugs in development.
SOURCE: U.S. Pharmacist, (1993) 18/11 (105).
ISSN: 0148-4818 CODEN: USPHD5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L169 ANSWER 39 OF 39 EMBASE
on STN
ACCESSION NUMBER: 92025751 EMBASE
DOCUMENT NUMBER: 1992025751
TITLE: Psychopharmacology of Alzheimer's disease.

AUTHOR: Sevush S.
CORPORATE SOURCE: University of Miami School of Medicine, Center on Adult Development and Aging, 1400 NW 10th Avenue, Miami, FL 33136, United States
SOURCE: Hospital Formulary, (1991) 26/11 (846-852).
ISSN: 0098-6909 CODEN: HOFOD
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

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=> fil medl; d que l23
FILE 'MEDLINE' ENTERED AT 13:33:10 ON 20 AUG 2004

 FILE LAST UPDATED: 19 AUG 2004 (20040819/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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claim 15

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L1        17224 SEA FILE=MEDLINE ABB=ON  NERVE GROWTH FACTORS+NT/CT
L4        28089 SEA FILE=MEDLINE ABB=ON  SLEEP DISORDERS+NT/CT
L5          636 SEA FILE=MEDLINE ABB=ON  TENSION HEADACHE/CT
L6         5604 SEA FILE=MEDLINE ABB=ON  CONSTIPATION/CT
L7         2501 SEA FILE=MEDLINE ABB=ON  FATIGUE SYNDROME, CHRONIC/CT
L8           77 SEA FILE=MEDLINE ABB=ON  COLD(1A)SWEAT?
L9         3767 SEA FILE=MEDLINE ABB=ON  SWEATING/CT
L19        7232 SEA FILE=MEDLINE ABB=ON  L1(L)(AD OR PD OR PK OR TU)/CT
L23           4 SEA FILE=MEDLINE ABB=ON  L19 AND (L4 OR L5 OR L6 OR L7 OR L8
                 OR L9)

=> s l23 not (l20 or l22)
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previously printed

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L170          4 L23 NOT (L20 OR L22)

=> fil embase; d que l72; d que l78; d que l79; d que l80

FILE 'EMBASE' ENTERED AT 13:33:12 ON 20 AUG 2004
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 FILE COVERS 1974 TO 19 Aug 2004 (20040819/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L43        1912 SEA FILE=EMBASE ABB=ON  TENSION HEADACHE/CT
L45        2843 SEA FILE=EMBASE ABB=ON  CHRONIC FATIGUE SYNDROME/CT
L46        5903 SEA FILE=EMBASE ABB=ON  SWEATING/CT
L47          97 SEA FILE=EMBASE ABB=ON  COLD(2A)SWEAT?
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L72           2 SEA FILE=EMBASE ABB=ON  L49 AND (L43 OR (L45 OR L46 OR L47))



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L42       46421 SEA FILE=EMBASE ABB=ON  SLEEP DISORDER+NT/CT
L44       14942 SEA FILE=EMBASE ABB=ON  CONSTIPATION/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L73        4408 SEA FILE=EMBASE ABB=ON  L42(L)(DT OR PC)/CT
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L74        1619 SEA FILE=EMBASE ABB=ON  L44(L)(DT OR PC)/CT
L78           1 SEA FILE=EMBASE ABB=ON  L49 AND L73 AND L74



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L42       46421 SEA FILE=EMBASE ABB=ON  SLEEP DISORDER+NT/CT
L44       14942 SEA FILE=EMBASE ABB=ON  CONSTIPATION/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L73        4408 SEA FILE=EMBASE ABB=ON  L42(L)(DT OR PC)/CT
L74        1619 SEA FILE=EMBASE ABB=ON  L44(L)(DT OR PC)/CT
L79           5 SEA FILE=EMBASE ABB=ON  L49/MAJ AND (L73 OR L74)



L24       18154 SEA FILE=EMBASE ABB=ON  NEUROTROPHIC FACTOR+NT/CT
L42       46421 SEA FILE=EMBASE ABB=ON  SLEEP DISORDER+NT/CT
L44       14942 SEA FILE=EMBASE ABB=ON  CONSTIPATION/CT
L49        3065 SEA FILE=EMBASE ABB=ON  L24(L)(AD OR DO OR PD OR PK OR DT)/CT
L73        4408 SEA FILE=EMBASE ABB=ON  L42(L)(DT OR PC)/CT
L74        1619 SEA FILE=EMBASE ABB=ON  L44(L)(DT OR PC)/CT
L80           6 SEA FILE=EMBASE ABB=ON  L49 AND (L73/MAJ OR L74/MAJ)

=> s (l72 or l78-l80) not (l60 or l63 or l64)

L171          9 (L72 OR (L78 OR L79 OR L80)) NOT (L60 OR L63 OR L64)

=> fil drugu; d que l116

FILE 'DRUGU' ENTERED AT 13:33:13 ON 20 AUG 2004
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FILE LAST UPDATED: 19 AUG 2004        <20040819/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<

>>>  A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED
     IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED
     ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
     STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
     EDITION).
     FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide



L100        690 SEA FILE=DRUGU ABB=ON  NERVE -GROWTH-FACTOR/CT OR NERVE-GROWTH
                -FACTOR/CT OR NERVE-GROWTH-FACTOR/CT
L101        106 SEA FILE=DRUGU ABB=ON  NEUROTROPHIC-FACTOR/CT OR NEUROTROPHIN?/
                CT
L109       9094 SEA FILE=DRUGU ABB=ON  SLEEP+NT/CT
L110         65 SEA FILE=DRUGU ABB=ON  TENSION/CT AND HEADACHE/CT
L111       6333 SEA FILE=DRUGU ABB=ON  CONSTIPATION/CT
L112          3 SEA FILE=DRUGU ABB=ON  CHRONIC-FATIGUE-SYNDROME/CT
L113         81 SEA FILE=DRUGU ABB=ON  FATIGUE-SYNDROME/CT OR FATIGUE/CT
L114       2540 SEA FILE=DRUGU ABB=ON  SWEATING/CT
L116          3 SEA FILE=DRUGU ABB=ON  (L100 OR L101) AND (L109 OR L110 OR
                L111 OR L112 OR L113 OR L114)
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previously printed

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=> fil capl wpids; d que l140; d que l142

FILE 'CAPLUS' ENTERED AT 13:33:15 ON 20 AUG 2004
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L117      21524 SEA (NERVE OR NEURON?)(2A) (GROWTH FACTOR#) OR NEUROTROPHIC
                FACTOR# OR NEUREGULIN# OR NEUROTROPHIN# OR GLIAL MATURATION
                FACTOR#
L128         25 SEA COLD(2A) SWEAT?
L140          2 SEA L117 AND L128



L117      21524 SEA (NERVE OR NEURON?)(2A) (GROWTH FACTOR#) OR NEUROTROPHIC
                FACTOR# OR NEUREGULIN# OR NEUROTROPHIN# OR GLIAL MATURATION
                FACTOR#
L123       3573 SEA SLEEP (3A) DISORDER#
L124       3270 SEA DYSSOMNIA? OR PARASOMNIA? OR JET LAG OR JETLAG OR APNEA#
                OR NARCOLEP? OR CATAPLEX? OR SOMNAMBULI?
L125        358 SEA TENSION(2A)(HEADACHE# OR HEAD(A) ACHE#)
L126       2706 SEA CONSTIPAT? OR OBSTIPAT? OR DYSCHEZI?
L127       1387 SEA CHRONIC(1A) FATIGUE
L141       2234 SEA L117(10A)(ADMIN? OR THERAP? OR PHARMAC? OR TREAT?)
L142         24 SEA L141 AND (L123 OR L124 OR L125 OR L126 OR L127)

=> s (l140 or l142) not (l158 or l161)   previously printed

L172         12 (L140 OR L142) NOT (L158 OR L161)

=> dup rem l170,l171,l172
FILE 'MEDLINE' ENTERED AT 13:33:40 ON 20 AUG 2004

FILE 'EMBASE' ENTERED AT 13:33:40 ON 20 AUG 2004
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PROCESSING COMPLETED FOR L170
PROCESSING COMPLETED FOR L171
PROCESSING COMPLETED FOR L172
L173         21 DUP REM L170 L171 L172 (4 DUPLICATES REMOVED)
                ANSWERS '1-4' FROM FILE MEDLINE
                ANSWERS '5-11' FROM FILE EMBASE
                ANSWERS '12-19' FROM FILE CAPLUS
                ANSWERS '20-21' FROM FILE WPIDS

=> d ibib ed ab 1-21; fil hom

L173 ANSWER 1 OF 21     MEDLINE on STN                  DUPLICATE 2
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ACCESSION NUMBER: 2003290887 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12818279
TITLE: Neurotrophin-3 improves functional constipation.
AUTHOR: Parkman Henry P; Rao Satish S C; Reynolds James C; Schiller Lawrence R; Wald Arnold; Miner Philip B; Lembo Anthony J; Gordon James M; Drossman Douglas A; Waltzman Lynn; Stambler Nancy; Cedarbaum Jesse M
CORPORATE SOURCE: Temple University Hospital, Philadelphia, Pennsylvania 19140, USA. (Functional Constipation Study Investigators).
SOURCE: American journal of gastroenterology, (2003 Jun) 98 (6) 1338-47.
Journal code: 0421030. ISSN: 0002-9270.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030624
Last Updated on STN: 20030806
Entered Medline: 20030805

ED Entered STN: 20030624
Last Updated on STN: 20030806
Entered Medline: 20030805

AB OBJECTIVE: Neurotrophin-3 (NT-3) is a neurotrophic factor involved in the growth, development, and function of the nervous system. In preliminary studies, s.c. recombinant methionyl-human NT-3 enhanced transit throughout the GI tract and increased stool frequency in normal and constipated subjects. Our aim was to assess 1) the dose-related effects of NT-3 on bowel function, colon transit, and symptoms of chronic constipation, and 2) its safety. METHODS: This was a double-blind, randomized, placebo-controlled phase II study. A total of 107 patients with a diagnosis of functional constipation (Rome II criteria) were randomized to receive 4 wk of double blind, s.c. injections of either placebo, 3 mg, or 9 mg NT-3 once per week (qW) or three times per week (TTW); or 9 mg NT-3 TTW for 1 wk, then qW. The primary endpoint was the change in number of spontaneous, complete bowel movements per week. Colon transit was assessed before and at end of treatment. RESULTS: Compared with placebo, patients who received 9 mg NT-3 TTW showed significant increases in frequency of spontaneous, complete bowel movements and total bowel movements, as well as dose-related softening of stool and improved ease of passage. The number of days per week without a bowel movement also decreased, colon transit improved, as did constipation-related symptoms. Weekly dosing was ineffective. Transient injection-site reactions, seen in one third of patients receiving NT-3 TTW, were the most frequent adverse event. CONCLUSIONS: NT-3, administered TTW, increased stool frequency, enhanced colon transit, and improved symptoms of chronic constipation. NT-3 seems to be a novel, safe, and effective agent for the treatment of functional constipation.

L173 ANSWER 2 OF 21 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000349412 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10889153
TITLE: Recombinant human neurotrophic factors accelerate colonic transit and relieve constipation in humans.
COMMENT: Comment in: Gastroenterology. 2000 Jul;119(1):257-60.
PubMed ID: 10889178
AUTHOR: Coulie B; Szarka L A; Camilleri M; Burton D D; McKinzie S; Stambler N; Cedarbaum J M
CORPORATE SOURCE: Gastroenterology Research Unit, Mayo Clinic and Mayo

Foundation, Rochester, Minnesota, USA.
CONTRACT NUMBER: K24-DK02638-01 (NIDDK)
R01-NS39722 (NINDS)
R01-DK54681-01 (NIDDK)
SOURCE: Gastroenterology, (2000 Jul) 119 (1) 41-50.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20010517
Entered Medline: 20000803
ED Entered STN: 20000811
Last Updated on STN: 20010517
Entered Medline: 20000803
AB BACKGROUND & AIMS: The aim of this study was to assess the effects of recombinant human brain-derived neurotrophic factor (r-metHuBDNF) and recombinant human neurotrophic factor 3 (r-metHuNT-3) on gastrointestinal motor functions in healthy people and in patients with constipation. METHODS: Gastrointestinal and colonic transit was measured by scintigraphy before and after 2 weeks of treatment. Daily diaries documented symptoms over 6 weeks before, during, and after treatment. In a randomized study of healthy subjects, 40 received 100 microg/kg r-metHuBDNF or placebo subcutaneously (SC) daily. In a separate study, 8 healthy subjects and 8 patients with constipation received 300 microg/kg r-metHuNT-3 SC thrice weekly. RESULTS: r-met-HuBDNF accelerated overall and proximal colonic emptying ($P<0.05$) in health. r-metHuNT-3 accelerated overall colonic transit in health and constipation (all $P<0.05$) and gastric and small bowel transit (both $P<0.05$) in health. r-metHuBDNF tended to increase stool frequency compared with placebo in health ($P = 0.09$). r-metHuNT-3 increased stool frequency ($P = 0.05$) and facilitated passage of stool ($P < 0.01$) in constipated patients. The effects on stool frequency started within 3 days of the beginning of neurotrophin administrations and lasted up to 5 days after treatment ended. r-metHu neurotrophic factors were well tolerated, although half of the participants in the 2 studies developed injection site reactions or paresthesiae. CONCLUSIONS: Exogenous neurotrophic factors stimulate human gut motility in health and constipation.

L173 ANSWER 3 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2004242315 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15140607
TITLE: Thy1 expression in the brain is affected by iron and is decreased in Restless Legs Syndrome.
AUTHOR: Wang Xinsheng; Wiesinger Jason; Beard John; Felt Barbara; Menzies Sharon; Earley Christopher; Allen Richard; Connor James
CORPORATE SOURCE: Department of Neural and Behavioral Science (H109), Penn State College of Medicine, 500 University Drive, Hershey, PA 17033, USA.
CONTRACT NUMBER: NS 042857 (NINDS)
NS 35088 (NINDS)
SOURCE: Journal of the neurological sciences, (2004 May 15) 220 (1-2) 59-66.
Journal code: 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040514
Last Updated on STN: 20040723
Entered Medline: 20040722

ED Entered STN: 20040514
Last Updated on STN: 20040723
Entered Medline: 20040722

AB Thy-1 is a cell adhesion molecule that plays a regulatory role in the vesicular release of neurotransmitters. The objective of this study is to examine the relationship between iron status and Thy1 expression in neuronal systems of varying complexity. Pheochromocytoma cell (PC12) cells were used to explore whether there was a direct relation between cellular iron status and Thy1 expression. Iron chelation significantly decreased expression of Thy1 in PC12 cells in a dose and time dependent manner. Transferrin receptor expression was increased with iron chelation demonstrating that a global decrease in protein synthesis could not account for the Thy1 changes. We also examined brain homogenates from adult rats that were nursed by dams on an iron deficient (ID) diet and found a significant decrease in Thy1 compared to control rats. Finally, the substantia nigra from individuals with Restless Legs Syndrome reportedly has lower than normal amounts of iron. Therefore, we examined this brain region from individuals with the clinical diagnosis of primary Restless Legs syndrome (RLS) and found the concentration of Thy1 was less than half that of controls. The results of these studies support the novel concept that there is a relationship between Thy1 and iron and point to a novel mechanism by which iron deficiency can affect brain function. They also indicate a possible mechanism by which iron deficiency compromises dopaminergic transmission in RLS, providing a potentially important link between decreased brain iron and the responsiveness to levodopa and iron supplementation treatment in RLS.

L173 ANSWER 4 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001416508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11464953
TITLE: A phase I/II trial of recombinant methionyl human brain derived neurotrophic factor administered by intrathecal infusion to patients with amyotrophic lateral sclerosis.
COMMENT: Comment in: Amyotroph Lateral Scler Other Motor Neuron Disord. 2000 Jun;1(3):141. PubMed ID: 11464948
AUTHOR: Ochs G; Penn R D; York M; Giess R; Beck M; Tonn J; Haigh J; Malta E; Traub M; Sendtner M; Toyka K V
CORPORATE SOURCE: Department of Neurology, Julius-Maximilians University, Wurzburg, Germany.
SOURCE: Amyotrophic lateral sclerosis and other motor neuron disorders : official publication of the World Federation of Neurology, Research Group on Motor Neuron Diseases, (2000 Jun) 1 (3) 201-6.
Journal code: 100964775. ISSN: 1466-0822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

ED Entered STN: 20010820

Last Updated on STN: 20010820
Entered Medline: 20010816

AB BACKGROUND: Brain derived neurotrophic factor (BDNF) is a potent survival factor for motoneurons. This study investigated the safety and tolerability of recombinant methionyl human BDNF (r-metHuBDNF) infused intrathecally by means of an implanted pump in patients with ALS. METHODS: Twenty-five patients with probable or definite ALS were treated with either r-metHuBDNF (25, 60, 150, 400 or 1000 microg/day) or placebo in a 12-week, randomized, double-blinded, sequential, dose-escalation study. Test treatment was interrupted by a washout period from days 11 to 25 to allow the evaluation of laboratory safety measures. In each dose cohort four patients received r-metHuBDNF and one received placebo. On completion of the double-blind period of the study all patients continued to receive r-metHuBDNF in an open-label extension for up to 60 weeks. Lumbar cerebrospinal fluid (CSF) samples were taken periodically from all patients for the measurement of r-metHuBDNF levels and in a minority of patients these were supplemented by cistemal samples. RESULTS: Within days after the initiation of infusion the majority of patients receiving r-metHuBDNF reported mild sensory symptoms, including paraesthesias or a sense of warmth, which were usually confined to the lower limbs and were frequently exacerbated by neck flexion. In most instances these symptoms decreased or even disappeared over several weeks. Sleep disturbance, dry mouth, agitation and other behavioural effects were encountered at higher doses (>150 microg/day) and necessitated dose reductions. The spinal CSF levels of r-metHuBDNF were directly related to dose, with a lumbar to cervical ratio of approximately 4:1. CONCLUSIONS: The intrathecal delivery of r-metHuBDNF in doses of up to 150 microg/day was well tolerated and appears feasible. The reversible CNS effects with higher dose indicate that BDNF can be delivered cranially against CSF flow. The small number of patients and the design of the study did not permit conclusions to be drawn about the efficacy of the treatment.

L173 ANSWER 5 OF 21 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003513669 EMBASE
TITLE: Neurotrophic factors and their receptors in human sensory neuropathies.
AUTHOR: Anand P.
CORPORATE SOURCE: P. Anand, Imperial College London, Department of Neurology, Hammersmith Hospital, Du Cane Road, London W12 ONN, United Kingdom. p.anand@imperial.ac.uk
SOURCE: Progress in Brain Research, (2004) 146/- (477-492).
Refs: 96
ISSN: 0079-6123 CODEN: PBRRA4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Neurotrophic factors may play key roles in pathophysiological mechanisms of human neuropathies. Nerve growth factor (NGF) is trophic to small-diameter sensory fibers and regulates nociception. This review focuses on sensory dysfunction and the potential of neurotrophic treatments. Genetic neuropathy. Mutations of the NGF high-affinity receptor tyrosine kinase A (Trk A) have been found in congenital insensitivity to pain and anhidrosis; these are likely to be partial loss-of-function mutations, as axon-reflex vasodilatation and sweating can be elicited albeit reduced, suggesting rhNGF could restore nociception in some patients. Leprous neuropathy. Decreased NGF in leprosy skin may

explain cutaneous hypoalgesia even with inflammation and rhNGF may restore sensation, as spared nerve fibers show Trk A-staining. Diabetic neuropathy. NGF is depleted in early human diabetic neuropathy skin, in correlation with dysfunction of nociceptor fibers. We proposed rhNGF prophylaxis may prevent diabetic foot ulceration. Clinical trials have been disappointed, probably related to difficulty delivering adequate doses and need for multiple trophic factors. NGF and glial cell line-derived neurotrophic factor (GDNF) are both produced by basal keratinocytes and neurotrophin (NT-3) by suprabasal keratinocytes: relative mRNA expression was significantly lower in early diabetic neuropathy skin compared to controls, for NGF (P<0.02), BDNF (P<0.05), NT-3 (P<0.05), GDNF (<0.02), but not NT4/5, Trk A or p75 neurotrophin receptor (all P>0.05). Posttranslational modifications of mature and pro-NGF may also affect bioactivity and immunoreactivity. A 53 kD band that could correspond to a prepro-NGF-like molecule was reduced in diabetic skin. Traumatic neuropathy and pain. While NGF levels are acutely reduced in injured nerve trunks, neuropathic patients with chronic skin hyperalgesia and allodynia show marked local increases of NGF levels; here anti-NGF agents may provide analgesia. Physiological combinations of NGF, NT-3 and GDNF, to mimic a 'surrogate target organ', may provide a novel 'homeostatic' approach to prevent the development and ameliorate intractable neuropathic pain (e.g., at painful amputation stumps).

L173 ANSWER 6 OF 21 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004268589 EMBASE
TITLE: New and emerging treatment options for chronic constipation.
AUTHOR: Schiller L.R.
CORPORATE SOURCE: Dr. L.R. Schiller, Baylor University Medical Center, Dallas, TX, United States
SOURCE: Reviews in Gastroenterological Disorders, (2004) 4/SUPPL. 2 (S43-S51).
Refs: 71
ISSN: 1533-001X CODEN: RGDEAK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Chronic constipation remains a therapeutic challenge for today's physicians. Traditional approaches include use of fiber, osmotic laxatives, stimulant laxatives, prokinetic agents, biofeedback training, and surgery. These often are tried sequentially and episodically and have little evidence of long-term efficacy. Patients often report inadequate relief of symptoms. There is room for improvement, therefore, in the therapy of chronic constipation. Future advances largely will be based on insights into the enteric nervous system (ENS), the structure and function of which is being revealed in great detail. Manipulating the ENS pharmacologically offers the opportunity to reprogram this key control system to improve bowel function. For example, interneurons in the ENS display 5-HT(4) receptors, activation of which enhances the peristaltic reflex. Prokinetic agents that stimulate those receptors, such as tegaserod and prucalopride, have demonstrated efficacy as investigational agents for the treatment of chronic constipation in large studies. Less well studied investigational drugs with presumed activity in the ENS include opiate antagonists and the nerve growth factor neurotrophin-3. Both of these types of agents have been shown to be effective in small groups of patients with constipation. Another approach under development

is to stimulate colonic fluid secretion by opening chloride channels in the epithelium pharmacologically. Existing nonpharmacological treatments that can be improved include biofeedback training for pelvic floor dysfunction and surgery. Future developments include investigation of electrical stimulation of the colon and use of stem cells to repopulate degenerated populations of neurons, interstitial cells of Cajal, or smooth muscle cells. .COPYRGT. 2004 MedReviews, LLC.

L173 ANSWER 7 OF 21 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004268583 EMBASE
TITLE: Chronic constipation.
AUTHOR: Talley N.J.
CORPORATE SOURCE: Dr. N.J. Talley, Clin. Enteric Neurosci. Trans./Epid., Mayo Clinic College of Medicine, Mayo Clinic, Rochester, MN, United States
SOURCE: Reviews in Gastroenterological Disorders, (2004) 4/SUPPL. 2 (S1).
ISSN: 1533-001X CODEN: RGDEAK
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English

L173 ANSWER 8 OF 21 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003273117 EMBASE
TITLE: Constipation: Evaluation and treatment.
AUTHOR: Rao S.S.C.
CORPORATE SOURCE: Dr. S.S.C. Rao, Department of Internal Medicine, Univ. of Iowa Carver Coll. of Med., 200 Hawkins Drive, Iowa City, IA 52242, United States. satish-rao@uiowa.edu
SOURCE: Gastroenterology Clinics of North America, (2003) 32/2 (659-683).
Refs: 102
ISSN: 0889-8553 CODEN: GCNAEF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Constipation is a common clinical problem that comprises a constellation of symptoms that include excessive straining, hard stools, feeling of incomplete evacuation, use of digital maneuvers, or infrequent defecation. Although many conditions, such as metabolic problems, fiber deficiency, anorectal problems, and drugs, can cause constipation, when excluded functional constipation consists of two subtypes: slow-transit constipation and dyssynergic defecation. Some patients with irritable bowel syndrome may exhibit features of both types of constipation. The Rome criteria for functional constipation together with modifications proposed here for dyssynergic defecation may serve as useful guidelines for making a diagnosis. Recent advances in technology, together with a better understanding of the underlying mechanisms, have led to real progress in the diagnosis of this condition. Management options are limited, however, and evidence to support these treatments is only modest. The treatment is primarily medical; surgical options should be reserved for refractory disease and after careful diagnostic work-up. Although laxatives remain the mainstay of therapy, prokinetics that are

colon-selective are optimal for treating patients with slow-transit constipation, but they are not yet available for clinical use. Recent controlled trials, however, are promising. Biofeedback therapy is the preferred treatment for patients with dyssynergia, but is not widely available. In the near future, user-friendly biofeedback programs including home therapy may facilitate wider use of these methods for patients with dyssynergic defecation.

L173 ANSWER 9 OF 21 EMBASE
on STN
ACCESSION NUMBER: 2002297247 EMBASE
TITLE: Role of neurotrophins in inflammation of the gut.
AUTHOR: Reinshagen M.; Von Boyen G.; Adler G.; Steinkamp M.
CORPORATE SOURCE: M. Reinshagen, Department of Medicine I, University of Ulm, Robert-Koch-Strasse 8, 89081 Ulm, Germany. max.reinshagen@medizin.uni-ulm.de
SOURCE: Current Opinion in Investigational Drugs, (2002) 3/4 (565-568).
Refs: 37
ISSN: 1472-4472 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 048 Gastroenterology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
030 Pharmacology
038 Adverse Reactions Titles
029 Clinical Biochemistry
008 Neurology and Neurosurgery
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Until now neurotrophins like nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin (NT)-3 and neurotrophic factors like glial-derived neurotrophic factor (GDNF) have been almost exclusively investigated concerning their role in differentiation, growth and survival of specific neurons in the peripheral and central nervous system. However, in the last decade several non-neuronal functions of neurotrophins and neurotrophic factors have been characterized. In the gastrointestinal tract, neurotrophins and neutrophic factors regulate neuropeptide expression, interact with immunoregulatory cells and epithelial cells and regulate motility during inflammation. This highlights this new and complex regulatory system as important, and may lead to new options in the treatment of acute and chronic inflammation of the gut.

L173 ANSWER 10 OF 21 EMBASE
on STN
ACCESSION NUMBER: 2000100017 EMBASE
TITLE: Therapeutics in the neurorehabilitation of Parkinson's disease.
AUTHOR: Colcher A.; Stern M.B.
CORPORATE SOURCE: Dr. A. Colcher, Parkinson's Dis./Move. Disord. Ctr., Penn Neurological Institute, University of Pennsylvania, 330 South 9th Street, Philadelphia, PA 19107, United States
SOURCE: Neurorehabilitation and Neural Repair, (1999) 13/4 (205-218).
Refs: 84
ISSN: 0888-4390 CODEN: JNRHFV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine

037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Parkinson's disease (PD) affects 1 percent of the population over the age of 65. The number of people with this disorder is steadily rising. Therapy for PD remains primarily pharmacologic, with medications that target the depleted dopaminergic system being the mainstay of therapy. Surgical therapies, both ablative and stimulatory, are increasingly being used for patients with more advanced disease and/or complications of drug therapy. Experimental therapies aimed at restoring dopaminergic function and protecting dopaminergic cells are being studied. Alternate neurotransmitter systems are being evaluated as potential targets for therapy. Complete treatment of patients with PD utilizes education, physical therapy, support groups, and medication. When a comprehensive approach is used, PD is treatable and manageable.

L173 ANSWER 11 OF 21 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96193928 EMBASE
DOCUMENT NUMBER: 1996193928
TITLE: New hope for treatment of Lou Gehrig's disease.
AUTHOR: Piascik P.
CORPORATE SOURCE: University of Kentucky, College of Pharmacy, Dept. of Pharmacology/Exp. Therap.,Lexington, KY, United States
SOURCE: Journal of the American Pharmaceutical Association, (1996) 36/6 (355-356).
ISSN: 1086-5802 CODEN: JPHAF8
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L173 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:267260 CAPLUS
DOCUMENT NUMBER: 140:297533
TITLE: Peptides and related molecules that modulate nerve growth factor activity
INVENTOR(S): Boone, Thomas C.; Wild, Kenneth D., Jr.; Sitney, Karen C.; Min, Hosung; Kimmel, Bruce
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026329	A1	20040401	WO 2003-US29866	20030919

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004121959	A1	20040624	US 2003-666480	20030918
PRIORITY APPLN. INFO.:			US 2002-412524P	P 20020919
			US 2003-666480	A 20030918

OTHER SOURCE(S): MARPAT 140:297533
ED Entered STN: 01 Apr 2004
AB The present invention relates to certain biol. active peptides and polypeptides which can be used as therapeutics or prophylactics against diseases or disorders linked to nerve growth factor (NGF) as the causative agent. In one aspect of the present invention, pharmacol. active polypeptides comprising peptides linked to one or more Fc domains are provided.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L173 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:493405 CAPLUS
DOCUMENT NUMBER: 133:115131
TITLE: Methods of using a **neurotrophin** and its analogues for the **treatment** of gastrointestinal hypomotility disorders
INVENTOR(S): Cedarbraum, Jesse M.
PATENT ASSIGNEE(S): Regeneron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041719	A1	20000720	WO 2000-US682	20000111
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6656474	B1	20031202	US 1999-232171	19990115
CA 2360252	AA	20000720	CA 2000-2360252	20000111
EP 1146899	A1	20011024	EP 2000-908254	20000111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102767	T2	20020422	TR 2001-200102767	20000111
TR 200201875	T2	20020923	TR 2002-200201875	20000111
JP 2002534479	T2	20021015	JP 2000-593329	20000111
NZ 512968	A	20030926	NZ 2000-512968	20000111
NO 2001003493	A	20010917	NO 2001-3493	20010713
ZA 2001005799	A	20020124	ZA 2001-5799	20010713
PRIORITY APPLN. INFO.:			US 1999-232171	A 19990115
			WO 2000-US682	W 20000111

ED Entered STN: 21 Jul 2000
AB The present invention relates to methods for enhancing gastrointestinal motility. In particular, the invention relates to the use of neurotrophin-3 (I)and its analogs for enhancing gastrointestinal motility.

Methods of using I and its analogs for treating gastrointestinal hypomotility disorders are also provided. Healthy volunteers with constipation were treated with 300 .mu.g/kg recombinant I three times/wk, s.c., for a total of seven doses. I caused an increase in stool frequency, ease of passage, and softening in stool consistency. The onset of I-induced effects in bowel function was rapid (within 24 h) and lasted for several days after treatment ended.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L173 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:368885 CAPLUS
DOCUMENT NUMBER: 140:386047
TITLE: Cytomodulating peptides and methods for treating neurological disorders
INVENTOR(S): Iyer, Suhasini; Buelow, Roland; Lazarov, Mirella; Fong, Timothy
PATENT ASSIGNEE(S): Sangstat Medical Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037196	A2	20040506	WO 2003-US33602	20031024

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-421297P P 20021024
US 2002-431420P P 20021205
US 2003-470839P P 20030515

ED Entered STN: 06 May 2004
AB Compns. and methods are provided for inhibiting neuronal cell death and the loss of neuronal contacts resulting from acute and chronic neurol. disorders, including neurodegenerative and neuroinflammatory diseases. The compns. and methods utilize RDP-58 compns. capable of providing a direct neuroprotective effect on neuronal cells in conjunction with inhibition of autoimmune and inflammatory processes.

L173 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:796307 CAPLUS
DOCUMENT NUMBER: 139:271103
TITLE: Treatment methods using homeopathic preparations of growth factors
INVENTOR(S): Brewitt, Barbara A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Pat. Appl. 2002 49,422.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003191061	A1	20031009	US 2002-304635	20021126
US 5629286	A	19970513	US 1996-710040	19960910
US 6239105	B1	20010529	US 1999-251820	19990217
US 6485480	B1	20021126	US 2000-499230	20000207
US 2002071873	A1	20020613	US 2001-870132	20010529
US 2002049422	A1	20020425	US 2001-1367	20011030
PRIORITY APPLN. INFO.:			US 1994-221365 B2	19940331
			US 1995-488722 B1	19950608
			US 1996-710040 A2	19960910
			US 1997-855096 A3	19970513
			US 1999-251820 A1	19990217
			US 2000-499230 A2	20000207
			US 2001-870132 B2	20010529
			US 2001-1367 A2	20011030
			US 2000-255958P P	20001215

ED Entered STN: 10 Oct 2003
AB The present invention comprises homeopathic prepns. of growth factors, cyclins, and methods for their use. Disorders which may be effectively treated with the compns. of the present invention include chronic viral disorders, such as HIV, AIDS, chronic fatigue syndrome and Epstein-Barr viral infections, cancer, diabetes, depression, and autism. Homeopathic prepns. of growth factors and/or cyclins are preferably administered orally. In an alternative embodiment, patients are treated with radio frequency signals corresponding to homeopathic dilns. of growth factors.

L173 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:664610 CAPLUS
DOCUMENT NUMBER: 139:375140
TITLE: The role of peptides in treatment of psychiatric disorders
AUTHOR(S): Holsboer, F.
CORPORATE SOURCE: Max Planck Institute of Psychiatry, Munich, Germany
SOURCE: Journal of Neural Transmission, Supplement (2003), 64(Neuropsychopharmacology), 17-34
CODEN: JNTSD4; ISSN: 0303-6995
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 26 Aug 2003
AB A review on the role of neuropeptides in the treatment of psychiatric disorders. In affective disorders a no. of neuropeptides seem to be causally involved in development and course of illness, esp. CRH, AVP and substance P, whose receptors are now targeted with small mols. designed to reduce depressive and anxiety symptoms. Also neurotrophins, may have a distinct role in antidepressant action and possibly also in causation of depression. Schizophrenia-like symptoms are caused by neurotensin (NT), supporting the notion that drugs interfering with NT systems are potential antipsychotics. Finally, sleep disorders, currently treated with hypnotics, that have serious adverse effects can be targeted with neuropeptides.
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L173 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:586259 CAPLUS
DOCUMENT NUMBER: 135:339330
TITLE: NT-3 (Takeda/Regeneron/Amgen) Rudolf Urbanics

AUTHOR(S): Anon.
CORPORATE SOURCE: Biorex Research and Development Company, Veszprem-Szabadsagpuszta, H-8201, Hung.
SOURCE: IDrugs (2001), 4(7), 820-824
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 14 Aug 2001
AB A review, with refs. Regeneron, in collaboration with Amgen, is developing neurotrophin-3 (NT-3), a neuronal growth factor, for the potential treatment of neuropathies, as well as Parkinson's disease (PD). The product was inlicensed from Takeda Chem. Industries. By May 1999, Regeneron had started phase I/II trials in patients who suffer constipation due to spinal cord injury, PD or other medical conditions. Initial results, presented at the annual meeting of the American Gastroenterol. Assocn. in May 1999, showed that NT-3 exerted strong prokinetic effects, which are thought to be due to increased cholinergic activity and a decrease in NO transmission and no. of NO synthase-pos. neurons. By 1994, Amgen had begun phase I/II trials on behalf of Amgen-Regeneron Partners for NT-3 in the US and Canada for the potential treatment for peripheral neuropathies. The mechanism by which NT-3 excites intestinal muscle is thought to involve increased non-cholinergic contractility, decreased non-adrenergic, non-cholinergic inhibitory neurotransmission, and a redn. in the no. of NOS-pos. neurons.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L173 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:227684 CAPLUS
DOCUMENT NUMBER: 132:274820
TITLE: Cloning, expression, and **therapeutic** use of artemin, a novel **neurotrophic factor**
INVENTOR(S): Milbrandt, Jeffrey D.; Baloh, Robert H.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018799	A1	20000406	WO 1999-US22604	19990929
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6284540	B1	20010904	US 1998-220528	19981224
US 2002002269	A1	20020103	US 1998-220920	19981224
CA 2343927	AA	20000406	CA 1999-2343927	19990929
AU 9964054	A1	20000417	AU 1999-64054	19990929
AU 764531	B2	20030821		
EP 1028975	A1	20000823	EP 1999-951657	19990929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002534957	T2	20021022	JP 2000-572257		19990929
NZ 509490	A	20031031	NZ 1999-509490		19990929
PRIORITY APPLN. INFO.:			US 1998-163283	A	19980929
			US 1998-108148P	P	19981112
			US 1998-218698	A1	19981222
			WO 1999-US22604	W	19990929

ED Entered STN: 07 Apr 2000

AB A novel growth factor, artemin, which belongs to the GDNF/neurturin/persephin family of growth factors, is disclosed. The human and mouse amino sequences have been identified. Human and mouse artemin genomic DNA sequences have been cloned and sequenced and the resp. cDNA sequences identified. The growth factors of the invention comprise an artemin amino acid sequence or a conservatively substituted variant thereof or a fragment thereof of at least 8 contiguous amino acids. In addn., methods for treating degenerative conditions using artemin polypeptides of the invention, methods for detecting artemin gene alterations and methods for detecting and monitoring patient levels of artemin are provided. Pan-growth factors comprising an artemin polypeptide of the invention and a fragment of at least one other growth factor from the TGF-.beta. family and nucleic acids encoding the pan-growth factors are also claimed. Compns. comprising an artemin polypeptide of the invention and a GFR.alpha. polypeptide are addnl. claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L173 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:323132 CAPLUS

DOCUMENT NUMBER: 129:23447

TITLE: A method for treating **tension**-type **headache**

INVENTOR(S): Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf

PATENT ASSIGNEE(S): Den.

SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819674	A2	19980514	WO 1997-DK502	19971104
WO 9819674	A3	19980716		
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748632	A1	19980529	AU 1997-48632	19971104
AU 734490	B2	20010614		
EP 1011656	A2	20000628	EP 1997-911150	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1132082	A1	20010912	EP 2000-204625	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

US 6284794	B1	20010904	US 1999-304115	19990504
US 2002072543	A1	20020613	US 2001-941855	20010830
US 6649605	B2	20031118		
US 2004097562	A1	20040520	US 2003-702497	20031107

PRIORITY APPLN. INFO.:

DK 1996-1243	A	19961105
US 1996-30294P	P	19961105
EP 1997-911150	A3	19971104
WO 1997-DK502	W	19971104
US 1998-85413P	P	19980514
US 1999-304115	A3	19990504
US 2001-941855	A3	20010830

ED Entered STN: 30 May 1998

AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. Gabapentin and dextromethorphan had a prophylactic effect on chronic tension-type headaches.

L173 ANSWER 20 OF 21 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-393363 [37] WPIDS
DOC. NO. CPI: C2003-104472
TITLE: Formulation useful for treating e.g. neurodynia, comprises a combination of e.g. antioxidant, antiinflammatory, circulatory enhancer, vasodilator, nerve growth factor, glycemic control, lipid reduction and mitochondrial activator.
DERWENT CLASS: B05
INVENTOR(S): GENERAL, R E; HARRIS, D H; MARTIN, R
PATENT ASSIGNEE(S): (GENE-I) GENERAL R E; (HARR-I) HARRIS D H; (MART-I) MARTIN R
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003028747	A1	20030410	(200337)*	EN	8

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2003068391 A1 20030410 (200340)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003028747	A1	WO 2002-US31469	20021003

US 2003068391 A1 Provisional US 2001-326784P 20011004
US 2002-264589 20021003

PRIORITY APPLN. INFO: US 2001-326784P 20011004; US 2002-264589 20021003

ED 20030612

AB WO2003028747 A UPAB: 20030612

NOVELTY - An ingestable nutrient formulation (F) comprises portion of antioxidant, antiinflammatory, circulatory enhancement, vasodilator, nerve growth, conduction and regeneration, glycemic control, sorbitol inhibitor, lipid reduction, mitochondrial activation or pancreatic stem cell support element.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an ingestable nutrient formulation comprising (wt.%):

(1) vitamin A (0.39);
(2) vitamin C (10);
(3) vitamin E (0.1);
(4) thiamin HCl (3.9);
(5) riboflavin (1);
(6) niacin (5.9);
(7) vitamin B6 (1.9);
(8) vitamin B12 (0.19);
(9) biotin (0.19);
(10) folic acid (0.08);
(11) magnesium (10);
(12) zinc (1.9);
(13) copper (0.05);
(14) acetyl-L-carnitine (19);
(15) horse chestnut extract (19);
(16) colostrum (10);
(17) L-taurine (4.9);
(18) butcher's broom root (3.9);
(19) alpha lipoic acid (2.9);
(20) betaine HCl (1);
(21) quercetin (0.39); and
(22) an inert ingredient (preferably magnesium stearate) (the remainder).

ACTIVITY - Vasotropic; Neuroprotective; Hypertensive; Analgesic; Osteopathic; Antidiarrheic; Antidiabetic; Laxative; Uropathic; Auditory; Tranquilizer.

MECHANISM OF ACTION - None given

USE - (F) is used in the treatment of conditions associated with complications arising from diabetes and circulatory problems (claimed). (F) is used for treating peripheral neuropathy, vascular insufficiency, numbness, burning feet, hypersensitivity, pins-and-needles sensations, tingling sensations, crawling and prickling sensations, pain, dizziness, muscle weakness, complications associated with dysglycemic, dysfunctional conditions e.g. varicose veins, peripheral vascular disease, phlebitis, intermittent claudication, vasculitis, spider veins, muscle wasting, nerve tissue atrophy, poor circulation, cold feet hyperesthesia, hip fracture secondary to falls associated with orthostatic hypotension, hypesthesia, neurodynia, impotence, diarrhea, **constipation**, sleeplessness due to nerve dysfunction, urinary incontinence and cardiovascular complications.

ADVANTAGE - (F) provides a unique combination of vitamins, minerals, herbs, amino acids and other elements that will stimulate the repair and growth of damaged nerve tissue, prevent nerve tissue dysfunction, restore blood vessel integrity, improve insulin production and reduce insulin resistance, support immunologic function, stimulate peripheral circulation, provide antioxidant nutrients to the nerves and blood vessels and help reduce lipid levels; reduce auto-oxidation of glucose causing a

reduction of cell destroying reactive oxygen species/free radicals; reduce formation of advanced glycation end products (AGEs) by nonenzymatic glycation of proteins, thus improving circulation capacity to all tissues including nerves; increase neuronal blood flow, indirectly leading to peripheral nerve oxygenation; reduce intracellular sorbitol accumulation; improve microcirculation at the level of the vasa nervorum; improve nerve cell growth and regeneration; provide antiinflammatory response; reduce the likelihood of future generations becoming diabetic; increase nerve transmission/conduction; improve glycemic control and therefore halt the progression of diabetes and its complications including neuropathy.
Dwg.0/0

L173 ANSWER 21 OF 21 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-607528 [69] WPIDS
DOC. NO. NON-CPI: N2001-453501
DOC. NO. CPI: C2001-180542
TITLE: Novel polynucleotide encoding human **nerve growth factor**-related G-protein coupled receptor for **treating** peripheral or central nervous system disorders and urinary incontinence.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): RAMAKRISHNAN, S
PATENT ASSIGNEE(S): (RAMA-I) RAMAKRISHNAN S; (FARB) BAYER AG
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001070954	A2	20010927	(200169)*	EN	83
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
US 2001041355	A1	20011115	(200172)		
AU 2001042513	A	20011003	(200210)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001070954	A2	WO 2001-EP3337	20010323
US 2001041355	A1 Provisional	US 2000-191766P	20000324
		US 2001-815333	20010323
AU 2001042513	A	AU 2001-42513	20010323

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001042513	A Based on	WO 2001070954

PRIORITY APPLN. INFO: US 2000-191766P 20000324; US 2001-815333 20010323
ED 20011126
AB WO 200170954 A UPAB: 20011126
NOVELTY - An isolated polynucleotide (I) encoding a human nerve growth factor-related G-protein coupled receptor (NGFR-GPCR) polypeptide (II) comprising a sequence having at least 50% identity to a sequence (S1) comprising 399 amino acids fully defined in the specification or S1, and comprising a sequence (S2) of 1400 nucleotides fully defined in the

specification, is new.

DETAILED DESCRIPTION - (I) comprises a sequence encoding (II), a sequence comprising S2, a sequence which hybridizes under stringent conditions to the above said sequences, a sequence which deviated from the above said sequences due to the degeneration of genetic code, or a fragment, derivative or allelic variant of the above said polynucleotide sequences.

INDEPENDENT CLAIMS are also included for the following:

(1) an expression vector (III) containing (I);

(2) a host cell (IV) containing (III);

(3) a substantially purified NGFR-GPCR polypeptide (II) encoded by (I);

(4) producing (II);

(5) detecting (M1) (I) or (II), by contacting a biological sample with a reagent which specifically interacts with (I) or (II);

(6) a diagnostic kit for conducting (M1);

(7) reducing the activity of NGFR-GPCR, by contacting a cell with a reagent which specifically binds to (I) or (II), such that the activity of NGFR-GPCR is reduced;

(8) screening (M2) for agents which decrease/regulate the activity of a NGFR-GPCR;

(9) a reagent (R) that modulates the activity of (I) or (II), identified by (M2); and

(10) a pharmaceutical composition (PC) comprising (III) or (R).

ACTIVITY - Antiparkinsonian; antibacterial; fungicide; protozoacide; virucide; analgesic; cytostatic; antiasthmatic; cardiant; hypotensive; hypertensive; osteopathic; antianginal; antiulcer; antiallergic; neuroprotective; anti-HIV; tranquilizer; neuroleptic; antimanic; antidepressant; nootropic; anticonvulsant; antidiuretic.

MECHANISM OF ACTION - Regulates NGFR-GPCR; antisense gene therapy. Antisense NGFR-GPCR oligonucleotides comprising at least 11 contiguous nucleotides of (I) was administered to a patient with a central nervous system (CNS) disorder. The severity of the patient's CNS disorder was found to be decreased.

USE - (I) is useful for detecting a polynucleotide encoding a NGFR-GPCR polypeptide in a biological sample, by hybridizing (I) to a nucleic acid material of a biological sample, to form a hybridization complex, and detecting the hybridization complex. Preferably, the nucleic acid material of the biological sample is amplified before hybridization. (II) is useful for screening agents which decrease the activity of NGFR-GPCR, by contacting a test compound with any NGFR-GPCR polypeptide encoded by (I), and detecting the binding of test compound with NGFR-GPCR polypeptide, where a test compound which binds to the polypeptide is identified as a potential therapeutic agent for decreasing the activity of NGFR-GPCR. (II) is useful for screening agents which regulate the activity of NGFR-GPCR, by contacting a test compound with NGFR-GPCR polypeptide encoded by (I), and detecting NGFR-GPCR activity of the polypeptide, where a test compound that increases the NGFR-GPCR activity is identified as a potential therapeutic agent for increasing the activity of the polypeptide, and where a test compound that decreases activity of the polypeptide is identified as a potential therapeutic agent for decreasing the activity of the polypeptide. (I) is useful for screening agents which decrease the activity of NGFR-GPCR, by contacting a test compound with (I), and detecting binding of the test compound to the polynucleotide, where a test compound which binds to the polynucleotide is identified as a potential therapeutic agent for decreasing the activity of NGFR-GPCR. PC is useful for modulating the activity of NGFR-GPCR in a disease e.g. peripheral or central nervous system, and urinary incontinence (claimed). NGFR-GPCR gene product is useful for preventing, ameliorating or correcting dysfunctions or diseases including infections such as bacterial, fungal, protozoan and viral infections, particularly those caused by HIV viruses, cancers, anorexia, bulimia, asthma, urinary

retention, angina pectoris, hypotension, hypertension, myocardial infarction, acute heart failure, osteoporosis, ulcers, allergies, benign prostatic hypertrophy, central or periphery nervous system disorders including primary and secondary disorders after brain injury, disorders of mood, anxiety disorders, disorders of thought and volition, **disorders** of **sleep** and wakefulness, diseases of the motor unit-like neurogenic and myopathic disorders, neurodegenerative disorders like Alzheimer's and Parkinson's disease, disorders leading to peripheral and chronic pain. (II) is useful as a bait protein in a two-hybrid assay or a three-hybrid assay, to identify other proteins which bind to or interact with NGFR-GPCR polypeptide and modulate its activity. (II) is useful for raising antibodies which can block the receptor and prevent the ligand binding.
Dwg.0/4

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